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THE SURGICAL TREATMENT OF PURE PULMONIC STENOSIS

A DESCRIPTION OF AN EXPANSIBLE VALVULOTOME

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ALTHOUGH stenosis of the pulmonary valve associated with some other lesion is one of the most frequently encountered congenital cardiovascular defects, isolated, or pure, pulmonic stenosis is a relatively rare disease. It has been only recently that operative procedures have been devised for its treatment. Brock,[1] in 1948, described a method of pulmonary valvulotomy which he carried out on three patients. In August, 1949,[2] he recorded the results of ten subsequent operations. Blalock and Kieffer[3] later reported a series of nineteen cases in which the Brock method was used, and Potts and associates[4] recently reported the outcome of four cases in which the operative procedure was based on the principle of the Brock operation but in which a different valvulotome was used. Although Brock's initial mortality rate was high, his later results, along with those of other workers mentioned, have been much improved.

The terms "pure" or "isolated," when applied to pulmonic stenosis, indicate absence of an associated cardiac lesion and are customarily used to denote pulmonic stenosis without interventricular septal defect. One might consider the terms misused in this sense because pulmonic stenosis without interventricular septal defect is often accompanied by a patent foramen ovale or by an interauricular septal defect due to the elevated right auricular pressure.

Stenosis of the pulmonary valve may be either of two types: the so-called valvular type, in which the valve cusps themselves are fused, or the infundibular or subvalvular type, in which the pulmonary conus or infundibulum of the right ventricle is hypertrophied and stenosed. While the latter type occurs rather frequently in patients with tetralogy of Fallot, it is thought to occur relatively infrequently in those with pure pulmonic stenosis. This is indeed fortunate because infundibular stenosis does not lend itself to valvulotomy, although attempts have been made to create a larger opening by excising a portion of the hypertrophied infundibular tissue. Cyanosis, which occurs only

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in the presence of a patent foramen ovale, depends upon the volume of blood shunted from the right to the left side. The degree of cyanosis, therefore, is directly related to the size of the foramen and to the degree of stenosis. Cyanosis is usually severe if the defect is large and the stenosis marked. It might be minimal or might be present only during exertion if the stenosis is mild and the septal defect small.

At first glance one would expect a systemic pulmonary anastomosis to benefit these patients, but, as Blalock and Kieffer[3] have pointed out, this procedure increases the pulmonary venous return to the left auricle, thus diminishing the blood flow through the patent foramen ovale, which has served as an overflow valve for the right side of the heart. This change in blood flow is likely to cause postoperative right-sided heart failure.

The diagnosis of pure pulmonic stenosis usually presents no problem for someone trained in the diagnosis of patients with congenital cardiac lesions. Occasionally, however, it might be difficult to differentiate this deformity from the tetralogy of Fallot. Cyanosis is usually absent during the first month of life. If the foramen ovale remains patent, the cyanosis may become intense as the patient becomes older. If it closes, cyanosis does not occur. These patients are often extremely incapacitated and frequently become very dyspneic on the slightest exertion. Clubbing of the fingers may or may not be present. On physical examination there may be bulging of the precordium due to the markedly enlarged and dilated right ventricle. Cardiac enlargement is nearly always present, predominantly on the right side. A systolic thrill and a murmur are usually present. The liver may be enlarged and pulsating. In the more severe cases right-sided failure with peripheral edema and ascites frequently occurs.

Roentgenologic examination reveals enlargement of both the right auricle and right ventricle and a full pulmonary conus. The pulmonary artery is enlarged. In older patients the right ventricle is frequently so enlarged that it touches the anterior chest wall. The electrocardiogram shows right axis deviation and right ventricular hypertrophy. The circulation time may be diminished if the foramen ovale is patent, but it may be normal or prolonged if the foramen ovale is closed. Cardiac catheterization reveals a high right ventricular pressure, a low pulmonary arterial pressure, and a diminished pulmonary blood flow. Dye injected for angiocardiographic examination appears early in the aorta if the foramen ovale is patent but lingers in the right ventricle if the foramen is closed.

OPERATIVE TECHNIQUE

In our first case we used an operative technique identical with that developed by Brock. We felt, however, that his valvulotome presented certain slight disadvantages. First, a large defect is made in the wall of the ventricle when the largest of the valvulotomes is passed through this structure into the pulmonic valve. The same may be said for the pulmonary artery sound. We used a large, curved hemostat to dilate the incised valve since we could not obtain a

pulmonary artery sound. Spreading the hemostat not only increased the size of the incision in the ventricle but resulted in considerable blood loss. We felt that an instrument with a small diameter which could be passed through the ventricle and expanded after the valve was engaged might present certain advantages. Thus we devised an instrument with six spring steel dilating elements which are pivoted at either end and which curve convexly when pressure is applied through a flexible shaft. We felt that this instrument might tear the lines of fusion of the valve leaflets; however, we have been unable to prove this. We used this instrument on the second patient with satisfactory results but were unable to use it on the third because the heart was too small to

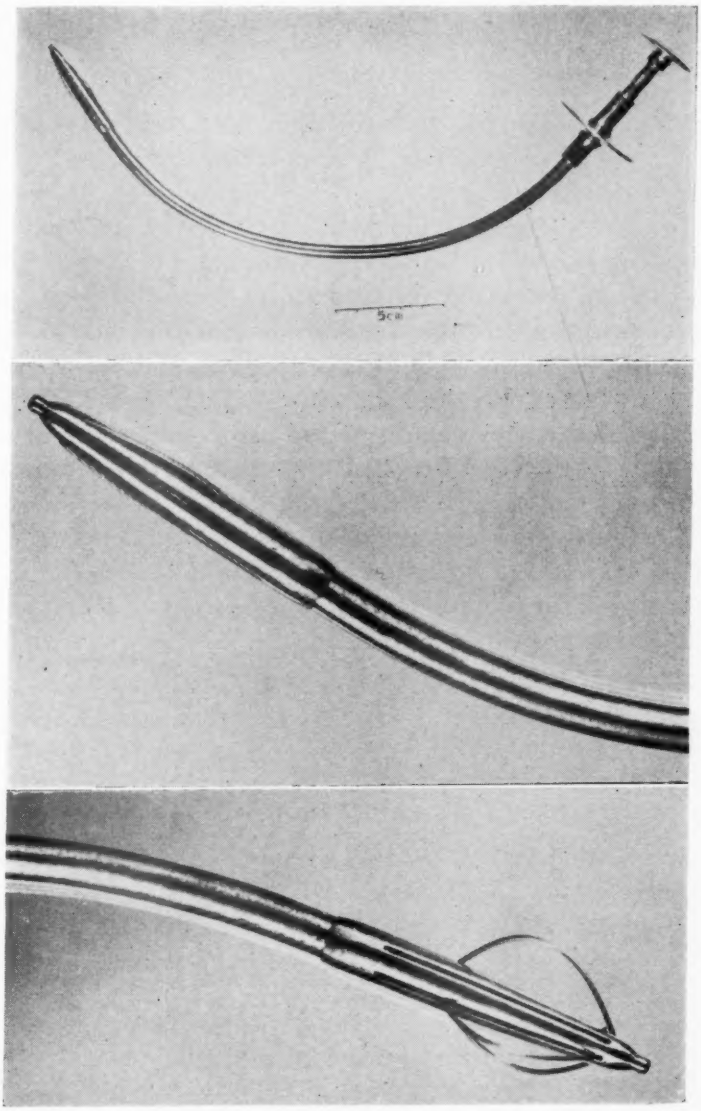

Fig. 1.—Photographs of the instrument used to open stenotic pulmonic valve. *A*, Over-all view of instrument; *B*, close-up view of leading end with dilating mechanism closed; *C*, close-up view of leading end with dilating mechanism open.

accommodate the instrument. We have since constructed a smaller instrument for use in smaller children and have reduced the number of wire dilating components from six to three (Fig. 1).

The operative technique which we employ at the present time is as follows: The patient is given penicillin, 300,000 units every six hours, and a proper dosage of quinidine for two days prior to operation. Pre-anesthesia medication of scopolamine and morphine sulfate is given. An anesthetic consisting usually of cyclopropane, oxygen, and ether is administered. The patient is placed in the supine position on the operating table with the left shoulder slightly elevated and the left arm flexed at the elbow so that the axilla is accessible. An anterolateral incision is started at the sternum and extended well into the axilla over the course of the third intercostal space. At times the costal cartilage of the fourth rib must be divided in order to facilitate exposure of the right ventricle. About 10 c.c. of 4 per cent Novocain is then injected into the pericardial cavity and allowed to remain for about five minutes before the pericardium is entered. The pericardium is then incised longitudinally about 1 cm. anterior to the phrenic nerve and held open with stay sutures. Novocain is injected into the right ventricular wall about 2 or 3 cm. from the origin of the pulmonary artery, and two stay sutures are placed in the ventricular muscle. With a sharp pointed knife an incision is made through the full thickness of the ventricular wall (Fig. 2). Bleeding is controlled with the finger. The valvulotome is then slipped into this opening, and the stenosed orifice is usually located with ease. Pressure is applied to the plunger of the valvulotome and the valve is enlarged to the size of the main pulmonary artery (Fig. 3). The valvulotome is then withdrawn and the opening in the ventricle is closed with several interrupted silk sutures. Gelatin foam is tied over the area of closure. The thrill has in all instances remained but has been much less intense than before removal of the obstruction. No diastolic thrill has been noted. The pericardium is closed loosely to allow drainage into the pleural cavity, and the chest is closed with silk sutures.

An intrapleural catheter is placed in the midaxillary line, and waterseal drainage is maintained until drainage has ceased and until the lung is completely expanded. Five hundred thousand units of penicillin are placed in the pleural cavity. The procedure is not particularly difficult and is usually well tolerated by the patient. Quinidine is given for the first three or four days postoperatively and penicillin is administered for approximately a week. Oxygen is required in most instances only during the first twenty-four hours after operation. Ambulation may be begun on the fourth or fifth day.

PRESENTATION OF CASE MATERIAL*

CASE 1.—R. W., a well-developed, well-nourished 6-year-old white girl, was admitted on May 21, 1950, with a diagnosis of pure pulmonic stenosis. She had a history of cyanosis at birth, which disappeared after several months and recurred only with crying. She had

*These patients were studied and their cases diagnosed at the Cardiac Clinic of the Los Angeles County General Hospital by Dr. George C. Griffith, Dr. Richard Cosby, Dr. David Levinson, and Dr. Willard Zinn. The diagnostic aspects of this deformity and more detailed case histories will be reported by them in a separate publication.

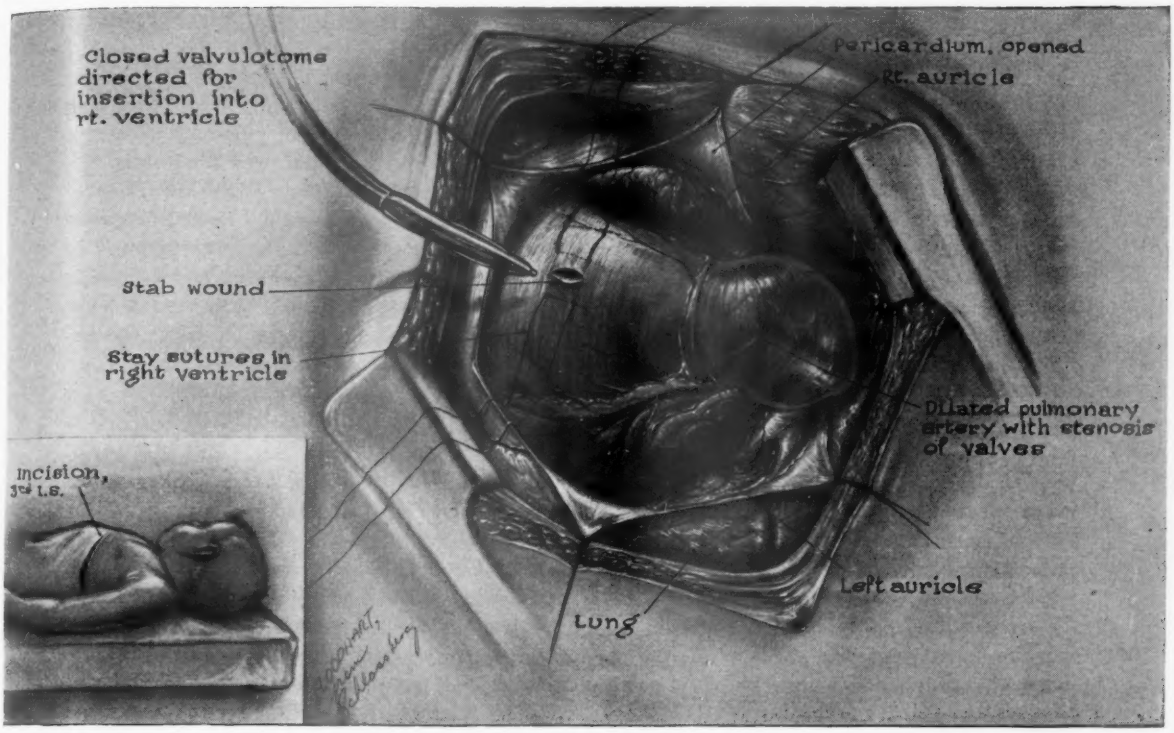

Fig. 2.—Illustration of heart showing pericardial incision, right ventricle, and markedly dilated pulmonary artery. A stab wound has been made between stay sutures, and the point of the instrument is poised for entry into the right ventricle.

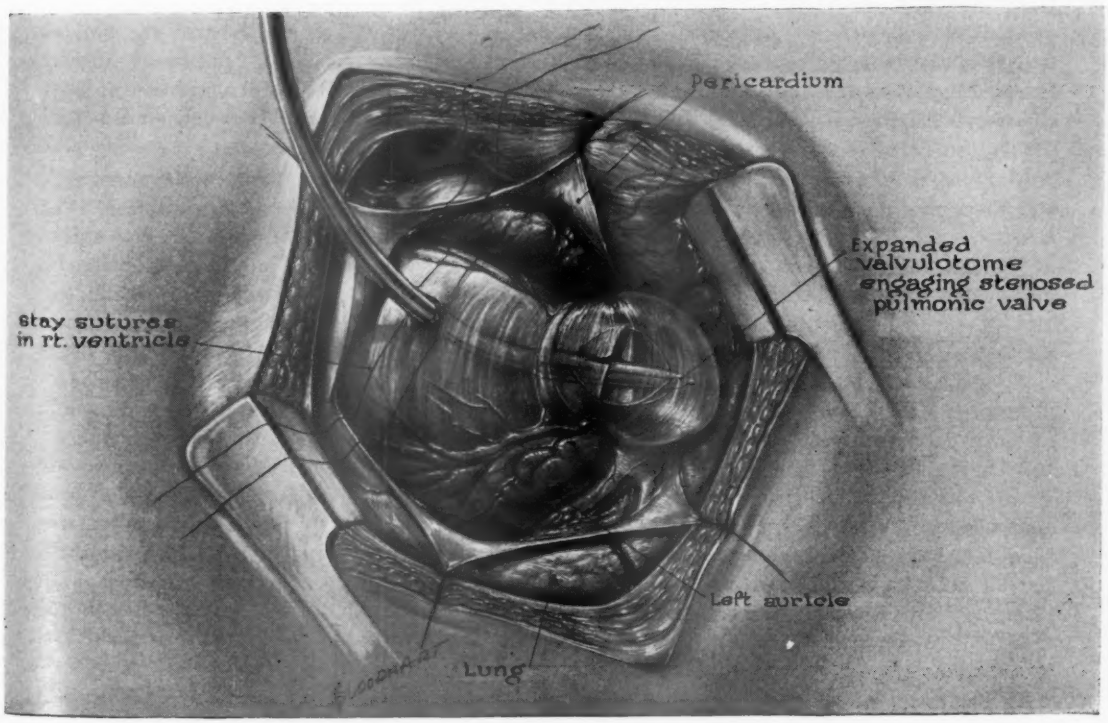

Fig. 3.—Illustration of instrument in right ventricle engaging stenotic pulmonic valve. The dilating mechanism is open, and there is dilatation and tearing of the pulmonic valve.

severe exercise intolerance, but her development otherwise had been essentially normal. A harsh murmur, discovered in infancy, persisted until the present time.

Physical examination revealed faint cyanosis about the mucous membranes. The chest was symmetrical and the lungs were clear to percussion and auscultation. The heart was generally enlarged to percussion. A systolic thrill could be felt over the pulmonic area and a harsh systolic murmur could be heard over the entire precordium but was loudest in the pulmonic area. Blood pressure was 110/70. The fingers were moderately clubbed. Electrocardiogram showed right axis deviation and right ventricular preponderance. Roentgenograms exhibited generalized cardiac enlargement, more prominent on the right, and enlargement in the region of the pulmonary artery. The hemoglobin was 13.5 Gm. per 100 c.c., and the white blood cells numbered 8,500 per c. mm. A pulmonary arterial pressure of 30/15 and a right ventricular pressure of 180/15 were demonstrated by cardiac catheterization. The femoral arterial saturation was 15.02 volumes per cent or 89.6 per cent saturated.

The patient was believed to have pure pulmonic valvular stenosis with a patent foramen ovale and was operated upon on June 5, 1950. An anterolateral incision was made in the third left intercostal space. The knife used had a double-edged blade but was otherwise similar to that described by Potts. This knife passed so easily through the stenotic orifice that it was difficult to determine when the valve was engaged. Thus, the Brock valvulotomes were introduced. Moderate force was required to pass the largest one into the pulmonary artery because the instrument impinged on the pulmonic valve. A medium-sized curved hemostat was then passed through the incised valve and spread in order to dilate it. This resulted in moderate blood loss since the ventricular opening was spread also. Following the valvulotomy the thrill in the pulmonary artery, which was previously pronounced, became considerably less intense. The postoperative course was not remarkable. The patient was discharged from the hospital on June 18, 1950, thirteen days following the operation. When seen about three months later, she was much improved. Exercise tolerance was almost normal and she no longer had exertional dyspnea.

CASE 2.—D. R., a well-developed 30-year-old white woman, was admitted on Oct. 4, 1950, with a chief complaint of mild exertional dyspnea all her life. History revealed that she had had essentially no symptoms until about the age of 15, at which time she noticed very mild shortness of breath upon exertion. She was told that she had a loud heart murmur but no diagnosis was made at that time. Her symptoms progressed little during the subsequent 15 years until the present time. She denied ever having been cyanotic. Physical and mental development was entirely normal.

Physical examination disclosed no evidence of cyanosis. The chest was symmetrical, and there was no respiratory lag. The lungs were clear to percussion and auscultation. The heart was not enlarged to percussion. A systolic thrill could be felt in the left anterior aspect of the chest over the pulmonic area. A harsh blowing systolic murmur, loudest in the pulmonic area, could be heard over the entire precordium. There was minimal clubbing of the fingers.

Roentgenologic examination showed a normal-sized heart with a convex prominence in the region of the pulmonary artery. Electrocardiogram showed sinus tachycardia and slight right axis deviation. The hemoglobin was 14.8 Gm. Cardiac catheterization revealed a pulmonary arterial pressure of 16/4 and a right ventricular pressure of 110/0. A diagnosis of pure pulmonic stenosis was made. On Oct. 9, 1950, she was operated upon through an incision in the left anterior third intercostal space. There was tremendous poststenotic dilatation. The valvulotome which we had devised was passed through the wall of the right ventricle into the pulmonary valve. The valve, which was only 3 to 4 mm. in diameter, was then enlarged to the size of the main pulmonary artery. Following this procedure the thrill in the main pulmonary artery, which had been markedly intense, greatly diminished in intensity. The patient's postoperative course was entirely uneventful, and she was discharged from the hospital on October 21, twelve days following the procedure. At this time she had no complaints.

She returned 1 week later complaining of pain in the chest and fever. Physical examination at that time showed essentially the same findings as at the time of her discharge.

However there were crackling râles at both bases and the heart was slightly enlarged to percussion. Temperature was 102° F. Roentgenograms of the chest showed a generally larger cardiac shadow than at the time of her discharge. There were patchy areas of infiltration in both lower lung fields and in the hilar regions.

Blood for culture was taken, and she was given penicillin intramuscularly. Temperature returned to normal temporarily but then rose each day to about 101°, and she still complained of pain in the chest. The penicillin was increased to 10 million units a day, but the temperature continued to be elevated. Sedimentation rate was 30. The medication was changed to aureomycin, and the temperature returned to normal, where it remained. Multiple blood cultures failed to reveal any organisms. She was given digitoxin several days after admission, whereupon the heart became much smaller and remained so. She was discharged on Dec. 16, 1950, again without complaints.

CASE 3.—M. M., the third patient, was a well-developed, well-nourished 4-year-old white girl, who was admitted on Oct. 10, 1950, with a history of cyanosis at birth. The cyanosis lasted for about 1 month, after which time it appeared only with exertion. Her development was nearly normal. She had severe exercise intolerance and, at the time of admission, could walk only about one block before becoming extremely fatigued.

The patient when admitted was in no acute distress and did not appear chronically ill. Physical examination at rest disclosed no signs of cyanosis; however, upon exertion mild cyanosis appeared. The chest was symmetrical, and there was no respiratory lag. A systolic thrill could be felt in the pulmonic area, and a harsh systolic murmur, loudest in the pulmonic area, could be heard over the entire precordium. The heart was not enlarged to the left to percussion. There was no clubbing of the fingers. The roentgenologic examination demonstrated enlargement of the heart, both to the right and to the left, and a full pulmonary conus. The electrocardiogram showed right axis deviation. Cardiac catheterization revealed a right ventricular pressure of 85/15 and a pulmonary arterial pressure of 20/10. The hemoglobin was 13.5 Gm. per 100 c.c. A diagnosis of pure pulmonic stenosis was made.

On October 16, an exploratory thoracotomy was carried out through the left third anterior intercostal space. There was moderate poststenotic dilatation of the pulmonary artery. An attempt was made to pass the valvulotome into the right ventricle, but the instrument appeared to be too large for this heart. Thus, the double-bladed knife was passed into the stenosed valve, and the valve was divided. It was dilated with a curved hemostat. The pulmonary arterial thrill, which had been intense, strikingly diminished in intensity. The patient's postoperative course was uneventful, and she was discharged free of complaints on Oct. 28, 1950.

DISCUSSION

Although no long-term results are yet available, valvulotomy appears to be a satisfactory treatment for pure pulmonic stenosis. The efficacy of the procedure can be evaluated only after consideration of such factors as the degree of pulmonary insufficiency produced and the possible effect of such insufficiency on the right ventricular muscle. Until the past few years valvulotomy for mitral stenosis was approached upon the premise that insufficiency is much better tolerated by the heart than is stenosis. This assumption has since been refuted, and today division of the mitral valve is designed to relieve the mechanical obstruction while producing a minimum of insufficiency. The anatomic characteristics of the pulmonic valve do not allow the development of an operation of similar design. One would think, however, that the right ventricle, because of its much lower blood pressure, could withstand an insufficient lesion much more satisfactorily than could the left ventricle.

The post-mortem appearance of two pulmonic valves which had been divided with the Brock valvulotome suggested to Blalock and Kieffer that the divided valve might function as a reasonably competent bicuspid valve.

In our patients a diastolic thrill or murmur has not been discernible following division of the stenotic valve, although a systolic murmur of much lower pitch has persisted. This observation agrees with the reports of others on this procedure.

We have not had an opportunity to see in what manner the instrument which we have devised enlarges the stenotic diaphragm. It is possible that it only dilates the valve, but we feel that it may also tear the lines of fusion of the cusps. Such tearing, however, is unlikely because the valve is tremendously scarred and thickened.

As to the ultimate fate of a valve treated in this manner, one can only speculate. One would hope that endothelization might rapidly occur and that the incision or tear might be permanent. We may find that our instrument in itself is not sufficient to relieve the obstruction permanently. We are now designing a slender valvulotome with small blades on its leading end, which can be manipulated to a cutting position after entrance has been gained into the right ventricle. Following actual incision of the valve leaflets with such an instrument our present one might be useful for dilating the incised valve.

From a technical point of view the procedure generally presents no major problems. It is rapidly executed and is well tolerated by the patients. However, one must be constantly aware of the possibility of serious hemorrhage, and every precaution must be taken to prevent it.

The progressively decreasing mortality rate and the high incidence of improvement following valvulotomy for pure pulmonic stenosis should recommend its use as the treatment of choice for patients with this deformity.

SUMMARY

Pulmonic valvulotomy has been employed by Brock and others for the treatment of pure pulmonic stenosis.

A valvulotome with a mechanism which may be manipulated into position after the instrument has been passed into the right ventricle is described.

The operative technique which we employed is discussed.

Three cases in which pulmonary valvulotomy was performed are presented.

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EXPERIMENTAL PRODUCTION AND CLOSURE OF ATRIAL SEPTAL DEFECTS, WITH OBSERVATIONS OF PHYSIOLOGIC EFFECTS

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THE development of operations which partially correct the circulatory deficiency in the tetralogy of Fallot has encouraged a consideration of analogous surgical procedures for other cardiac diseases, both congenital and acquired. In the fall of 1947, Dr. H. B. Burchell and Dr. J. E. Edwards pointed out to one of us that congenital heart disease with complete transposition of the great vessels might be benefited by the establishment of a communication between the 2 atria. In cases of complete transposition the blood is oxygenated normally and reaches the left atrium but cannot be delivered to the peripheral tissues because the vascular trunk for that purpose is misplaced. The blood is pumped from the left ventricle back again to the lungs.

More recently Hanlon and Blalock have analyzed the data in the literature on cases of complete transposition and have described 23 of their own. They divided the entire group of 128 cases into 7 categories, which were based on the presence of associated cardiac anomalies. They concluded from their investigation that "An interventricular septal defect is the single compensating abnormality associated with the largest life expectancy," and that a "Patent interatrial septum is the next most favorable isolated defect and the combination of these two gives the best prognosis of all."

Hanlon and Blalock implied that the results of their analysis are of limited applicability to corrective procedures since the term "patent foramen ovale" indicates "any interatrial septal defect." Presumably information is not available regarding the effect on longevity of various sized atrial defects.

There are 2 other congenital heart diseases that might be benefited by the creation of an interatrial communication, namely, atresia of the mitral valve and atresia of the aortic valve. The circulatory abnormalities in these conditions have been described by Edwards. In both there is adequate pulmonary flow and oxygenation of the blood. The difficulty arises from the failure of this oxygenated blood to reach the systemic vessels after gaining the left atrium or ventricle. Usually a small atrial defect does exist through which blood may flow from left to right and from here to the systemic circuit via the pulmonary artery and a patent ductus arteriosus. Surgical enlargement of the atrial defect should be considered as a possible therapeutic measure.

Hanlon and Blalock have described a method of anastomosing the right superior pulmonary vein to the right atrium, or to the superior vena cava

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after excision of the azygos vein, thus causing a mixing of blood from two blood circuits. The course of the blood through the surgical anastomosis in these animals simulates that in an atrial or a ventricular defect. The operation of Hanlon and Blalock conceivably could be of benefit to a person with complete transposition or to one with atresia of the aortic or mitral valve.

The studies described here were begun in the fall of 1947. They were done entirely on dogs with the end in view of producing large atrial septal defects and observing their physiologic effects.

It was hoped that the animals with an interatrial communication might in time exhibit circulatory disturbances similar to those seen in patients with atrial defects and that physiologic studies on the animal might illuminate some of the obscurities of the human condition. Finally, it was thought that it might be possible to close the defects surgically.

The anatomy of the cardiac region with which we are concerned is more easily understood if reference is made to the photographs showing the defects produced (Figs. 1 and 2). Descriptions of the surgical procedures were made with the animal lying on its left side and with the surgeon facing the abdomen, the animal's head lying to his right.

PRODUCTION OF ATRIAL SEPTAL DEFECTS

Description of the Most Suitable Operation, Series A.—This was a "blind" method, the heart remaining full of blood during the procedure. With the positioning of the animal as given in the previous paragraph and with the external cardiac landmarks identified, the pericardium was opened ventral and parallel to the phrenic nerve, and was suspended from the margins of the incision by means of 2 or 3 linen sutures. The tip of the right auricular appendage was then picked up with a smooth forceps and a cotton ligature was placed loosely about it. A long-bladed knife with a pared-down handle was then introduced into the auricular appendage and the cotton ligature was secured about the handle. The auricular tip was then held up by the ligature or forceps with the left hand. Care being exercised not to cut the atrial wall, the knife tip was advanced to the posterior margin of the atrial septum and pushed through this structure. The defect was then created by cutting in a cephalic direction for a distance of 1 cm. or less. The knife was withdrawn and, if necessary, the cotton ligature about the auricular appendage was tied. Usually the edges of the auricular incision were held together with a serrefine clamp, and after several minutes no further bleeding took place and the need of repairing the hole in the tip of the auricular appendage was obviated.

Occasionally, rhythmic disturbance such as tachycardia, auricular fibrillation, and apparent atrioventricular dissociation appeared, but these were transient in all cases. Originally, procaine solution was placed on the surface of the heart, but it was later found unnecessary.

The defect was examined directly by feeling it through the lateral right atrial wall, or examined digitally, and in some instances enlarged, by the index finger of the right hand invaginating the right auricular appendage. It was also possible, although this obstructed intracardiac flow and caused a

sharp drop in carotid blood pressure, to place the index finger across the front of the great vessels, invaginate the left auricular appendage and feel the defect. It was the custom not to close the pericardium until the defect had been palpated by the surgeon and the assistants.

The operation did not induce great changes in carotid or right atrial blood pressure although extrasystoles were evident in the tracings.

It was possible to make a number of mistakes, the most obvious of which was cutting in the wrong area of the septum. In exploring the defect it was also possible to be too vigorous and push the finger through the atrial wall. The actual incision of the septum and its palpation occupied 5 minutes; the entire operation required about 30 minutes for completion.

Immediately after the defect had been made, a bruit might be felt and a murmur heard on the right lateral atrial wall opposite the cephalic end of the cut septum. This was not observed in all cases and it was not determined why some defects resulted in bruits and some did not. A crude endocardioscope was employed to look into the right atrium in some acute experiments, and a turbulent flow of bright red blood just below the cephalic edge of the atrial septal defect could be seen.

The operation (series A) was performed 9 times with 2 postoperative deaths. One death was due to a pleural infection; the cause of the other was not clear. Both animals that died after operation exhibited defects in the atrial septum measuring 1.25 by 1.25 cm. The operative mortality rate was 22 per cent. Of the remaining 7 animals, 5 have since come to necropsy. Three of the 5 exhibited defects of significant size (Fig. 1, *a* and *b*). One atrial septum did not appear to have been cut and another had the appearance of a scar which had closed over an incision. The success of the operation was thus 3 in 5 (60 per cent). Two of the animals are still alive and well 18 months after operation.

Of the 5 animals killed after the operation, 4 had been submitted to catheterization of the right side of the heart in an attempt to demonstrate the defect by passing the catheter through it. This was successfully accomplished in 3 cases. In the animal in which catheterization was unsuccessful necropsy later revealed that a defect did not exist.

Operation in Series B.—This was an earlier series in which operation had been performed before the possibilities and ease of the approach through the auricular appendage were realized. In this operation the lateral right atrial wall was opened between 2 silk stay sutures. With the sutures held up, little bleeding took place from the beating atrium. The knife was introduced into the chamber between the stay sutures and the septum was blindly incised.

There were 8 animals in this group, and there was 1 operative death from hemorrhage due to cutting through the lateral left atrial wall. One dog died of distemper on the tenth postoperative day and at necropsy showed mitral vegetative endocarditis, a dilated right ventricle, and an atrial septal defect measuring 10 by 19 mm. in an atrial area measuring 19 by 20 mm. The mortality rate was 25 per cent. The remaining 6 animals surviving the operation were killed subsequently.

In 3 animals, killed 3 months after operation, the defects made were uniformly small: 2 by 4 mm., 7 by 3 mm. and 7 by 4 mm., with corresponding septal areas of 15 by 17 mm., 15 by 15 mm. and 14 by 13 mm., respectively. The small size of the defects produced can be attributed to inexperience rather than to any inherent fault of the approach. In 2 of the 6 animals, killed 7 months after operation, the defect appeared to have healed spontaneously. In 1 animal no defect nor scar was seen. The success of the series must be put at 3 in 6 (50 per cent).

Production of Atrial Septal Defects Under Direct Vision by Temporary Interruption of the Circulation, Series C.—Umbilical tape was placed about the superior vena cava, the azygos vein, and the inferior vena cava. After

Fig. 1.—*a*, A defect was made by an incision in the atrial septum. The animal was killed 5 months after the operation. The defect is viewed from the right. *b*, Same animal as in *a*. The defect is viewed from the left atrium.

the pericardium had been opened and suspended from the margin of the incision, stay sutures were placed either on opposite ends or opposing sides of the proposed incision of the atrial wall; the latter gave the better exposure. With the time noted, the umbilical tapes were successively pulled and clamped with a hemostat to the tissues of the thorax, thus occluding the veins.

After the heart had been allowed a few beats to empty itself, the atrial wall was incised. In the great majority of instances an excellent view of the interior was obtained; the mouth of the coronary sinus and the muscular rim of the fossa ovalis could easily be seen. It was usually not difficult to pick up the atrial septum with a forceps and excise a section with scissors. The operative mortality rate was high: 8 deaths on the operating table in 14 operations. Two deaths resulted from cutting the wrong areas. Were this the only difficulty it would not constitute a deterrent to the operation, since additional experience and more detailed anatomic knowledge usually reduced

errors of that kind to a minimum. The chief cause of death in these operations was coronary air embolism, actually demonstrated in 2 animals and presumed in the others. The opening of the atrial septum exposes the left chamber of the heart to the atmosphere and, as is well known, a very small amount of air in the left side of the heart quickly causes death.[6, 10] A number of devices were employed to exclude air from the left chamber: flooding the area with line solution, allowing a small quantity of blood to cover the atrial area continuously, and digitally blocking the incised septal area. While these expedients were not entirely unsuccessful, none of them gave a satisfactory procedure. So great and frustrating did this matter of air embolism become that it led to a review of the literature on the subject of coronary air embolism. This in turn led to the tentative belief that all intracardiac procedures on the left side of the heart are liable to failure unless some means is obtained of precluding the entrance of air into the coronary vessels.

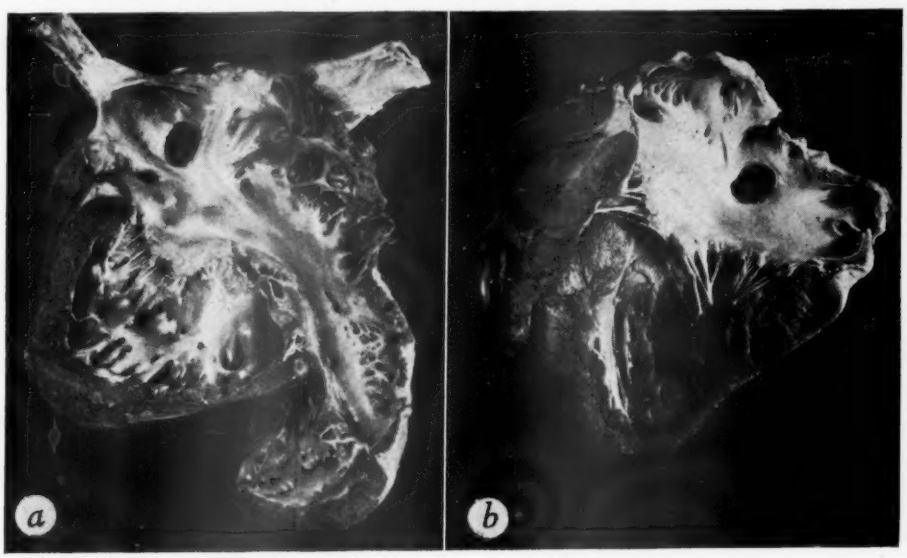

Fig. 2.—*a*, A defect was made by excising a portion of the atrial septal wall. The animal was killed 4 months after the operation. The heart is viewed from the right side. *b*, Same animal as in *a*. The heart is viewed from the left atrium.

Two additional animals showed signs of cerebral damage for one month after the operation. The duration of the occlusion of the preatrial venous trunks was 2 to 3½ minutes. By previous studies on this specific point these intervals of anoxia were known not to cause apparent cerebral damage. It was assumed that cerebral air embolism was the cause of the odd behavior of these 2 animals.

Although a failure surgically, the making of atrial defects by this method provided additional animals for physiologic measurements. Animals in series C (Fig. 2, *a* and *b*) and in series A only were used for physiologic studies.

A Fourth Method of Producing Atrial Septal Defects.—In an acute experiment a U-shaped row of sutures was placed in the lateral right atrial wall, each suture passing through the atrial chamber and also through the septal wall op-

posite. The open end of the U faced the right hilus and the limbs blocked off the flow of blood from the inferior and superior venae cavae. The right atrium was then opened in this relatively bloodless area and the septum was excised. The clamp devised by Blalock and Hanlon provides the same bloodless field in a more satisfactory manner.

SPONTANEOUS CLOSURE OF ATRIAL SEPTAL DEFECTS

There is an apparent tendency for artificially made atrial septal defects to close spontaneously. This is more pronounced the smaller the defect. The healing progresses from the caudal (inferior vena caval) end of the defect to the cephalic end. In some of the animals of series B, which had a small defect, complete healing was observed. Two of them exhibited only linear scars 10 mm. long when killed 7 months after the operation. Another of the same series, killed 3 months after operation, exhibited a defect measuring 2 by 4 mm. near the cephalic rim of the septal area and in addition a linear scar 7 mm. long extending toward the inferior vena cava. These scars were proved to be such by microscopic examination of sections.

Two other animals of the same series, killed 3 months after operation, did not exhibit scars in addition to their small defects.

In larger defects, as in the animals in series A, there appeared to be a lesser tendency to closure. Only 1 of the 4 animals in this series which had a defect and which came to necropsy exhibited an atrial septal scar. This was a dog with a defect measuring 5 by 6 mm. and a scar 4 mm. long extending caudal to this.

In the animals in series C, which had a piece of atrial septal tissue excised, spontaneous closure was not observed.

MEASUREMENTS OF CERTAIN PRESSURES AND OTHER FACTORS IN ANIMALS WITH SURGICALLY CREATED ATRIAL SEPTAL DEFECTS

Observations of Intracardiac Pressures.—Intracardiac pressures were measured with a water or mercury manometer. In all studies the animals were under pentobarbital sodium anesthesia. In the measurements in animals with closed chests a Cournand catheter cut to 60 cm., or a number 10 vinyl tubing of similar length, was used for reaching the right ventricle and pulmonary artery. The former was the only instrument that could be introduced through an atrial septal defect, and this was most easily done by employing the approach through the femoral vein and the inferior vena cava. It was not always possible to pass the vinyl tubing into the pulmonary artery. Entrance was sometimes possible if the tubing impinged on the right ventricular wall at the apex, doubled on itself, and entered the pulmonary artery in a bent condition. This bend was straightened out by pulling the tubing back and forth. By the injection of Thorotrast, the vinyl tubing was made radiopaque and its position was determined.

For the measurement of pressures in animals with closed chests it was necessary to establish a base line, particularly for the atrial pressures. A series of roentgenograms of 6 animals of various sizes was taken with a Cournand

radiopaque catheter in place passing from the superior to the inferior vena cava. In 4 cases the animal was placed on its left side and the rays passed from a ventral to a dorsal direction. The radiopaque catheter was superimposed on the animal's spinous processes. In the other 2 cases the catheter lay 9.4 and 5.7 mm., respectively, to the right of the spinal column. It was believed that this deviation of less than 1 cm. could be ignored. In all studies on animals with closed chests the animal was placed on its left side and the level of the fifth and sixth spinous processes was used as the base line.

In recording pressures from the cardiac chamber, the length of the tubing eliminate the excursions due to breathing. This latter influence is particularly reduced systolic pulsations; readings were taken at the end of expiration to apparent in the right atrium.

In measurements in animals with closed chests the right atrial position was determined by passing the catheter, connected to a water manometer, into the right ventricle and withdrawing it to a point where systolic pulsation ceased but where respiratory variations were still seen. The position of the catheter in the right ventricle and pulmonary artery was determined by roentgenoscopy. The left atrial position was found by roentgenoscopy and confirmed by withdrawing highly oxygenated blood. Considerable variation, depending on the placement of the catheter, was encountered in right ventricular pressures. Presumably the rapidly moving wall, chordae tendineae, and papillary muscles prevent the easy inflow and outflow of blood through the catheter tip which is necessary to measure pressure with a mercury or saline manometer. All of the recorded pressures presented in this report are averages of several consecutive manometric readings.

In one group of studies on animals with open chests the animals were on their backs and the sternum was split in the midline. The right and left auricular appendages were exposed by pericardial incisions and number 10 vinyl tubes (outside diameter 3 mm., inside diameter 2.6 mm.) were tied in each. About 1 cm. of the tube was projected into the chamber. Base lines were determined directly by holding another tube at the level of the inserted catheters. With the animal in the dorsal decubitus position the left atrium lies between 1 and 2 cm. dorsal to the right. After the placement of the catheters, the readings were taken alternately with the artificial respiration temporarily shut off.

Another method was to place the animal on its left side, expose the heart, and pass a number 10 vinyl tube into the right atrium via the jugular vein, and to insert another similar tube into the left atrium via a right pulmonary vein, which was entered at the hilus of the right lung.

For convenience, the data have been divided into 5 groups defined by the presence or absence of a defect and by the specific condition of the study.

The mean right atrial pressure was determined in 12 normal animals with closed chests. One animal had 4 and another had 2 determinations on separate days to make a total of 16 pressure observations. The values ranged from –5.4 cm. of water to 0. The average was –2 cm. of water. In 10 of these same animals the right ventricular pressure was determined during the same study.

In 2 animals 2 determinations of this pressure were made on separate days. These 12 values ranged from +5 to +10.4 mm. of mercury and averaged +7.6 mm. of mercury. There were 6 determinations of pulmonary arterial pressure in 5 animals. These values ranged from +6 to +16 mm. of mercury and averaged +10.6 mm. of mercury.

Pressure determinations were made on 4 animals with atrial septal defects which had been demonstrated by catheterization. The mean right atrial pressure was determined 3 times in 1 animal on separate days, and once in 3 other animals. The 6 pressure readings ranged from –1.7 to +1 cm. of water and averaged –0.8 cm. of water. Four readings of right ventricular pressure were made with a range of +4.6 to +16 mm. of mercury; the average was +9.2. Pulmonary arterial pressures ranged in 3 determinations from +7.6 to +23 mm. of mercury and averaged +15.2 mm. The left atrium was entered 3 times in as many animals. The pressure ranged from +3.4 to +5.4 cm. of water and averaged +4.3 cm. The right and left atrial pressures were taken within a few minutes of each other.

By subtracting the average values of the right atrial pressures from the average values of the left atrial pressures in the group just mentioned a difference of +5.1 cm. is obtained. This differs little from the average of the differences in the 2 pressures considered separately in the animals. This average is +5.4 cm. of water. The left pressure exceeded the right in all instances.

Additional data were accumulated on the matter of left and right atrial pressures in animals with proved defects. They were grouped separately since the animals were placed on their backs rather than on their sides. Three series of readings were made on 2 animals. The differences in the pressures of the 2 atria ranged from +1.4 to +5.4 cm. of water and averaged +3.1 cm. The difference between the average left and the average right atrial pressure was +3 cm. of water. In all instances the left atrial pressure exceeded the right; the readings were made within a few minutes of each other.

In animals with an open chest, respiration being supplied through an intratracheal cannula, the right atrial pressure was measured in 9 animals. The average was +3.8 cm. of water with a range of +2 to +5.1 cm. In 7 animals of the same series the left atrial pressure averaged +6.3 cm. of water with a range of +4 to +9 cm. In 6 of these determinations the pressures in the 2 chambers were measured within a few minutes of each other.

In 4 acute studies of animals with the chest open, pressure in the right and left atria was measured before and after the making of an atrial septal defect. The pressure in the left chamber exceeded that in the right in all instances, both before and after the defect was made. The changes in pressure in an individual chamber before and after the defect was created were not consistent. The pressures here reported have been summarized previously[12] (Table I). With some differences similar results have been reported by Little and associates.

Cardiac Size and Electrocardiograms.—Six animals with proved atrial septal defects have been observed for 6 months and have not exhibited any outstanding circulatory disturbance. Roentgenologic examination of the heart has

TABLE I. SUMMARY OF ATRIAL, RIGHT VENTRICULAR, AND PULMONARY ARTERIAL PRESSURES IN ANIMALS WITH CLOSED AND WITH OPEN CHESTS

	RIGHT ATRIUM, CM. OF WATER			LEFT ATRIUM, CM. OF WATER			RIGHT VENTRICLE, MM. OF MERCURY			PULMONARY ARTERY, MM. OF MERCURY		
	NO.*	RANGE	AVERAGE	NO.*	RANGE	AVERAGE	NO.*	RANGE	AVERAGE	NO.*	RANGE	AVERAGE
Normal animals												
Closed chest	16	−5.4 to 0	−2				12	+5 to +10.4	+7.6	6	+6 to +16	+10.6
Open chest	9	+2 to +5.1	+3.8	7	+4 to +9	+6.3						
Animals with atrial defects												
Closed chest	6	−1.7 to +1	−0.8	3	+3.4 to +5.4	+4.3	4	+4.6 to +16	+9.2	3	+7.6 to +23	+15.2
Closed chest (animal lying on back)	3	+3.8 to +8.2	+6.6	3	+6.2 to +13.6	+9.6						

*Number of observations.

not shown an increase in cardiac size. Electrocardiograms have not shown abnormalities. Circulation times tested in a few cases by the sodium cyanide method have been within the normal range.

Oxygen Content Studies of the Blood in Animals With Atrial Defects.—Catheterization of the right side of the heart was performed on 4 animals for the purpose of obtaining blood samples for analysis. The position of the catheter was determined by roentgenoscopy and by pressure measurements. The animals were all under pentobarbital sodium anesthesia. The blood samples were withdrawn under oil into syringes containing powdered heparin. They were analyzed in duplicate for oxygen content and in selected cases for oxygen capacity, the method of Van Slyke and Neill being used. In the animals used for this study the presence of an atrial defect had previously been determined by catheterization.

In 3 of the 4 animals a highly saturated sample of blood was found in the right atrium, possibly indicating a shunting of blood from the left to the right atrium. A deliberate attempt was made to place the tip of the catheter near the supposed location of the defect. Interest did not lie in obtaining a mixed atrial sample, as is the hope when one is calculating cardiac outputs. It lay rather in finding, if possible, an arterialized sample which would indicate that some transatrial flow was taking place. In the first animal the highest oxygen content of either the superior or the inferior vena cava was 13.3 volumes in 100 c.c., whereas the midatrial sample was 16.2 volumes in 100 c.c. of blood. Corresponding values in the second animal were 8.6 and 14, and in the third were 10.8 and 14.6 c.c. of oxygen per 100 c.c. of blood. The first value cited in each of these 3 pairs (13.3; 8.6; 10.8) is the highest of several from the inferior and superior venae cavae, the second (16.2; 14; 14.6) is the highest

in the middle of the right atrium near the supposed location of the atrial defect. All that can be said is that one right atrial sample exceeded the nearest vena caval sample by 2.9, 5.4, and 3.8 volumes of oxygen per 100 c.c. of blood, respectively. The literature is not uniform on what would constitute a significant difference,[9] and normal ranges of oxygen content of right atrial blood were not determined in this study. Although the evidence is not overwhelming, it indicates that a shunt of blood from the left to the right atrium did exist.

METHOD OF CLOSING ATRIAL SEPTAL DEFECTS

After the development of techniques for making an atrial communication in animals, attention was given to the possibility of surgically closing these defects. The attempt to develop such a closure was made with the hope of ultimate application to human patients. There exist human cases of cardiac failure apparently due entirely to the presence of a defect in the atrial septum which permits shunting of blood from the left to the right side of the heart. This has been established by clinical and pathologic observations.[5] It seems reasonable to believe that a closure of the defect would be at least partially curative. The closure of atrial defects, needless to say, would find application in an entirely different group of patients than those for whom the operation of making an atrial defect was suggested. The only similarities of the 2 groups are that both are congenital heart diseases, and both concern the same anatomic structure, the atrial septum.

Cohn proposed an ingenious method of bringing the right lateral atrial wall against the septum as a patch for the closure of atrial defects. Preliminary to his operation he approached the heart from the left side, opened the auricular appendage, forced a curved clamp through the septum, then opened and withdrew it. He produced defects from 4 to 6 mm. in diameter. Murray has described a method of drawing the edges of atrial and ventricular septal defects together by means of sutures passed from outside the heart, through the appropriate structure and out again. In addition to experimental studies he performed this operation once in a human case of atrial septal defect.

At first it was attempted to open the right atrium and to suture the edges of the previously made defect one to the other. Reference to the section on operative deaths in the series C animals will make it clear why making a communication from the atmosphere to the left chamber of the heart was attended with repeated operative deaths. In 1 animal that survived the operation death occurred 3 days postoperatively from infection. It was noted that the silk suture had pulled through the lower lip of the atrial defect. This discouraged further attempts at direct suture.

It seemed reasonable to believe that a graft of some sort could be introduced into the right atrium and brought into apposition to the septal defect without the necessity of excluding blood from the heart.

Studies on Graft Materials.—

Polythene sheeting: It was at first hoped that a thin sheet of Polythene, which has been found to be nonreactive with tissues,[2] could be employed as the

graft material. Operation was performed on 3 animals. In each instance an incision was made through the right side of the thorax and an atrial incision was effected according to the method given previously. The defect was then palpated digitally in each instance. Then, by a method described in the next section, a piece of Polythene sheeting (0.0005 cm. in thickness) measuring 1 by 1 or 1 by 2 cm. was introduced into the right atrium and properly positioned. All 3 animals stood the procedure well and appeared to be in excellent condition postoperatively.

It will be best to describe first the appearance at necropsy of the septum and graft in the animal allowed to survive 6 months. The sheet of Polythene had apparently become endothelized and was actually incorporated in the atrial septal wall. There was no clot on the sheet and no vegetations. Inspection of the lungs showed no signs of emboli. The operation considered as a whole was less than satisfactory, since the graft had been placed too far cephalad, rather than over the center of the atrial septal defect. The placement of the graft was not anatomically perfect; possibly it was physiologically effective in stopping the passage of blood through the defect.

While it might be true that at 6 months no ill effects from the grafts were detectable, the question naturally raised is: What is going on in the intervening period? Operation was performed on 2 additional animals in an attempt to answer this question.

It was known from acute physiologic studies that shortly after the graft was placed in the atrium a clot of about 2 mm. thickness formed over both sides of the sheet. This clot was dense but was loosely adherent to the surfaces of the Polythene. Any suture material left exposed in the atrium also quickly became covered with clot. On these, however, the tendency was for the formation of long streamers of clot.

An animal in which the defect was made and then repaired by use of a sheet of Polythene was killed 2 weeks after operation. At necropsy a clot was found which was firmly adherent to the Polythene, but grossly no endothelization nor organization had taken place. Another animal at 2 months after operation showed the clot on the graft to be about 50 per cent organized and endothelized.

It was concluded that a bare sheet of Polythene placed in the heart chamber quickly became covered with clot, and that this slowly became organized sometime between 2 and 6 months after operation.

Polythene sheeting graft covered with an inverted segment of vein: Because it was reasoned that the endothelium of a vessel would be the substance least likely to cause excessive clot formation, it was determined to excise a piece of vein, invert it, and slip the segment over the sheet of Polythene prior to its insertion into the right atrium. This practice proved so successful that all subsequent attempts at closure of atrial septal defects were performed with this technique. Two studies will be mentioned to illustrate the desirability of the inverted venous covering of the graft.

An atrial defect was made by incision and the Polythene-and-vein graft was inserted by the technique described in the next section. The venous

segment was obtained from the azygos vein. The animal was killed 1 month later (Fig. 3). A smooth surface resembling endothelium was found to cover the graft completely. A similar procedure was done on another animal which was killed 2 weeks after operation. Again apparently complete endothelization of the inserted sheet of Polythene had taken place. In some way the vein appears to enhance organization and smoothing of the surface. Sections did not show a layer of endothelium on these grafts but only a dense, smooth-surfaced connective tissue. The endothelial layer may have been removed in preparing the sections.

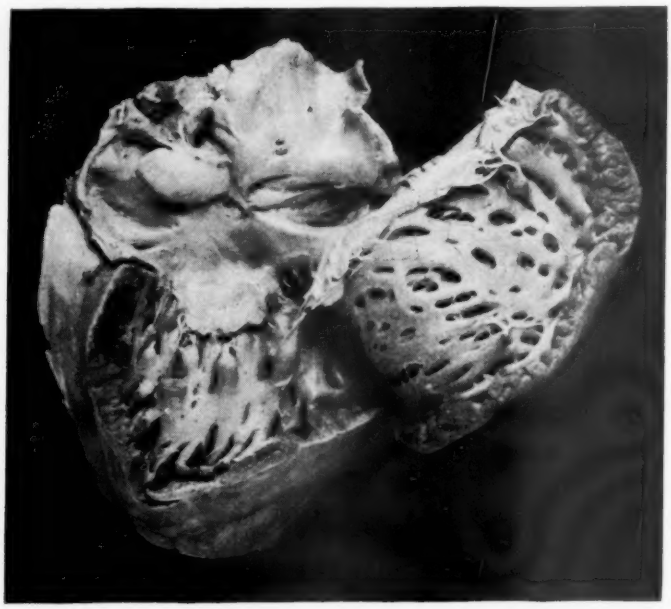

Fig. 3.—The atrial septal defect had been closed previously with a Polythene graft covered with an inverted segment of vein. The placement is fairly good.

As a result of these observations, it was concluded that when a piece of Polythene sheeting was to be placed in a heart chamber, the piece should first be covered with an inverted piece of vein.

The Technique of Closing an Atrial Septal Defect.—

Preparation and placement of the graft: After the defect was made it was digitally palpated by the surgeon and assistants. The graft was then introduced at the same operation. In 5 instances the sheet of Polythene was first covered with an excised piece of azygos vein, and in 3 instances the sheet of Polythene was introduced without covering. In the animals in which the segment of azygos was used, this vein was ligated just distal to its union with the superior vena cava and then ligated again about 3 cm. distal to this. The isolated segment was then excised, inverted, and slipped over the sheet of Polythene.

In general, 3 sutures were used to introduce the graft into the right atrium. One was placed in the edge destined to lie near the caudal end of the atrial septum and termed the caudal end of the graft, one in the cephalic end,

and one in the edge destined to fit near the dorsal margin of the atrial defect. Without the venous covering, of course, the sutures merely lay exposed; with the venous sleeve in place the knots tying the sutures to the sheet of Polythene and a part of the adjacent suture were covered by the venous sleeve. In some early instances the dorsal suture was omitted. However, experience indicated that it should be used. A straight needle was attached to the end of each of the 3 sutures. An additional knot for marking purposes was placed on each suture about 2 mm. from the graft (Fig. 4).

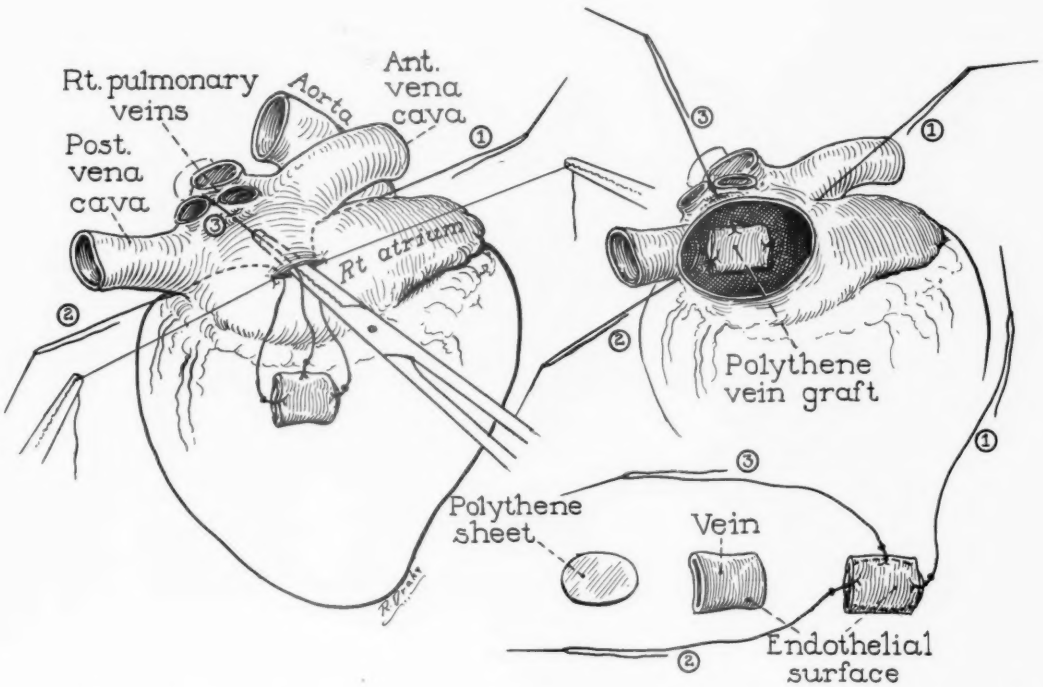

Fig. 4.—Stages in the operation for closure of the atrial defect. At the lower right is shown the Polythene-vein graft with the 3 sutures attached. At the upper left the graft is shown being introduced into the right atrial chamber. In the upper right drawing the lateral wall of the right atrium has been cut away and an idealized location of the graft is seen.

Location of the graft needles: The procedure was "blind," blood not being excluded from the heart. An incision 1 cm. long was made in the right lateral atrial wall. Bleeding from this incision was controlled by 2 silk stay sutures placed at either end. The 3 needles were successively introduced into the atrial chamber through the incision and brought out again through the atrial wall at 3 separate points. These points were all in the same plane as the atrial septum. The first, or cephalic, suture was passed out behind the right auricular appendage near the root of the aortic reflection; the second, or caudal, suture came out near the medial surface of the inferior vena cava; the third, or dorsal, suture emerged at the hilus of the right lung beyond the pericardial reflection but to the right of the pulmonary veins. The graft was introduced into the right atrium after the first 2 sutures had been passed. The sutures were pulled through until the knot which had been previously

placed 2 mm. from the graft could be seen or felt. The silk sutures were then anchored in place by tying them to the adjacent heart wall or contiguous tissues.

In many of the initial attempts the piece of Polythene was incorrectly placed. With experience, the landmarks became sufficiently familiar to allow the placing of the graft more nearly in the correct position. The knots already referred to were of great assistance in this regard.

Fig. 5.—Another defect and closure is seen from the left atrium. The probe lies in the caudal end of the defect and the partial occlusion of the cephalic half by the graft can be seen. The graft placement was fair.

The operation for closure of the defect was performed 8 times with 1 operative death. This occurred on the operating table and was due to hemorrhage which took place from the opening in the right lateral atrial wall. Venous covering for the graft was not used in 3 of the 7 animals surviving the operation.

An attempt was made to grade the success of placement of the graft. There was great variation in this placement and only occasionally was it entirely satisfactory. Fig. 5 shows a fair graft placement. It is believed that practice would improve this aspect of the operation. It is interesting that in specimens cut, opened, and inspected, the graft often seemed poorly placed, but when the heart was realigned in its normal position the graft covered the defect. One gained the impression that complete, perfect placement was perhaps unnecessary; that a reasonable approximation of the graft to the defect would establish a sufficient blockage to the flow of blood; in other words, that physiologic block was more easily obtained than anatomic block. Studies designed to test the effectiveness of the block were not carried out.

SUMMARY

The purpose of the work was to devise a technique for producing large atrial septal defects which could be applied to cases of human diseases. It has been established that there exist a variety of means of producing the atrial defects in dogs. Since the condition of complete transposition of the great vessels does not exist in dogs, nor is it experimentally producible, the experimenter is denied an opportunity to test the hypothesis that the atrial communication would be of benefit in that condition. This aspect must remain conjectural.

Sufficient measurements were made of left and right atrial pressures under a variety of conditions to enable one to conclude that mean left atrial pressure exceeds the right. The production of a bruit and murmur, and the samples of oxygenated blood withdrawn from the right atrium, constitute evidence that blood is in actual fact shunted from the left atrial chamber to the right in artificially produced defects.

It has been shown that Polythene sheeting covered with vein can be introduced into the heart without serious reaction. This is in general agreement with the experience of others employing Polythene in various parts of the body.

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SUPPURATIVE PELVIC THROMBOPHLEBITIS

I. Incidence, Pathology, and Etiology

A Study of 70 Patients Treated by Ligation of the Inferior Vena Cava and Ovarian Vessels

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DURING recent years the implications of intravascular clotting have broadened considerably. It is now generally recognized that there are two essential types, occurring typically in the deep venous system of the lower extremities. Thus, the concepts of Homans[1] and Ochsner and DeBakey[2] as to the occurrence of bland thrombosis or phlebothrombosis, on the one hand, and inflammatory thrombosis or thrombophlebitis, on the other, are now well established. Tendencies to embolism complicating these types of thrombosis differ greatly. In instances of phlebothrombosis, most often asymptomatic, there is a greater predisposition to infarction and fatal emboli because of loose attachment to the vein wall and friability of the clot, which is composed mainly of fibrin with an admixture of cellular elements. In contrast, an inflammatory reaction within the wall of the vein and clot in cases of thrombophlebitis tends to result in a firmer, adherent clot and greatly lessened incidence of lethal embolism.

The occurrence of clotting initially in the pelvic veins, due to severe infection, has received little attention in the recent medical literature. This condition may occur in patients with postabortal of post-partal infection, after gynecologic operations or intrauterine application of radium, or in connection with pelvic abscesses other than those associated with puerperal or postabortal infection.[3] The clots so formed are septic and tend more often to be frankly purulent. This process of liquefaction, therefore, predisposes to embolism. The resulting infected emboli tend to be small and are liberated in showers. Pyemia or septicemia with the development of metastatic abscesses results and is often fatal. This is in contradistinction to the fatal massive pulmonary embolism associated with phlebothrombosis. The process of septic thrombosis in the pelvic veins is a distinct type of intravascular clotting which has been termed "suppurative pelvic thrombophlebitis"; it is this pathologic entity with which this communication is concerned. Consideration of this type of clotting in a separate category seems warranted for several reasons. It can occur, as will be shown later, independently of thrombosis of the veins in the leg. More-

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over, repeated septic embolisms result in septicemia and seeding of small abscesses in distant organs rather than death from sudden massive pulmonary embolism.

Recognition of the occurrence of this type of thrombosis is by no means recent. Before the advent of specific antibacterial agents, the surgeons at the turn of this century were operating upon patients with puerperal pyemia. Investigators, such as Trendelenburg,[4] Miller,[5] and many others, were able to demonstrate thrombosed veins by palpation at operation. These surgeons ligated individual veins in the pelvis proximal to the thrombus. The ovarian, hypogastric, external iliac, and common iliac veins and the vena cava have been ligated individually, depending upon the site or sites of thrombi. Uninvolved tributaries of the vena cava or uninvolved ovarian veins were left undisturbed. The mortality rate after ligation, however, was only slightly better than following expectant therapy. Thus, ligation fell into disrepute. However, our experience has shown that surgical therapy can be highly successful in suppurative pelvic thrombophlebitis, even though exhaustive medical therapy has failed. This depends upon complete interruption of the venous return from the uterus, that is, the ovarian vessels and vena cava, which is effectively accomplished by ligation of the right and left ovarian vessels and inferior vena cava irrespective of the location of the thrombotic processes. Since our original report[6] of great improvement following ligation of the inferior vena cava and ovarian veins in 1 patient with suppurative pelvic thrombophlebitis, 70 such refractory cases have been managed in this way.

INCIDENCE

The recent introduction of sulfonamides and antibiotics has served to reduce the incidence and severity of pelvic sepsis. The success of chemotherapy and antibiotics depends, however, upon many factors, such as susceptibility of the invading organism or organisms, time of application of therapy, walling off of the infective process, and blood supply to the infected area. These variables cannot often be controlled in individual cases. Experience on the obstetric and gynecologic services of Charity Hospital in New Orleans has demonstrated that, in spite of these agents and the prophylactic or therapeutic use of anticoagulants, a number of severe cases of pelvic sepsis still occur. This, coupled with the fact that Charity Hospital serves as a salvage center for a large area, permits observation of many cases of this type.

The incidence of criminally induced abortion with repeated invasion of the uterus under most deplorable conditions is high in the neighboring area. Also, unhygienic surroundings in the home at the time of delivery or during the puerperium serve to increase the incidence of puerperal sepsis. Thus, examination of statistics from Charity Hospital[7] has shown that from July 1, 1937, to Jan. 1, 1946, 2.2 per cent of the cases from the gynecologic wards in which necropsy was done showed evidences of suppurative pelvic thrombophlebitis. From the obstetric wards during the same period 35 per cent of the patients who died of puerperal sepsis showed evidence of intravascular clotting at necropsy. Reports from other centers corroborate this definite inci-

dence of suppurative pelvic thrombophlebitis. In a study of the maternal deaths in New York City for 1947, Gold and Wallace[8] reported that 50 per cent of the deaths attributed to puerperal sepsis were due to embolic phenomena. Similarly, Zimmerman and associates,[9] in a review of 345 deaths associated with pulmonary embolism at the Michael Reese and Chicago Memorial Hospitals, reported that emboli occurring in the presence of suppurative thrombophlebitis were a contributory cause of death in 2.9 per cent of the cases.

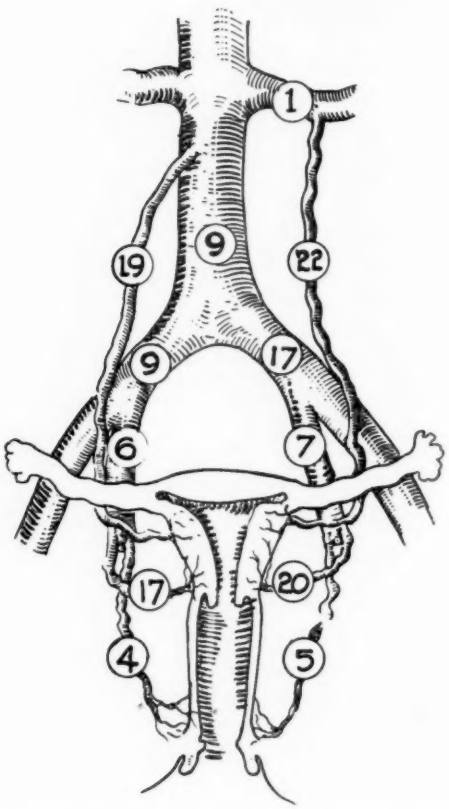


Fig. 1.—Sites of thrombi in 70 cases of suppurative pelvic thrombophlebitis.

PATHOLOGY

The present series has afforded a means of delineating some of the pathologic characteristics active in suppurative pelvic thrombophlebitis. The site of thrombosis was established by palpation at operation and, in many cases, by histologic examination of small resected portions of the ovarian vessels. Fig. 1 shows diagrammatically the topographic distribution of thrombi in the 70 patients in this series. It illustrates the fact that thrombi are almost equally distributed between the two primary highways of venous return, that is, the uterine draining into the hypogastric and common iliac veins and inferior vena cava, and the ovarian, draining directly into the inferior vena cava on the right side and indirectly by way of the left renal vein on the opposite side. It is to be emphasized that in the majority of cases thrombi were evident in

TABLE I. SITES OF THROMBOSIS IN 70 PATIENTS WITH SUPPURATIVE PELVIC THROMBOPHLEBITIS

Uterine (alone)	17
Ovarian (alone)	16
Combined uterine and ovarian	29
Common internal, external iliac (combined)	12

TABLE II. INCIDENCE OF THROMBOSED VEINS IN 70 PATIENTS WITH PELVIC SUPPURATIVE THROMBOPHLEBITIS

	RIGHT	LEFT	TOTAL
Inferior vena cava			9
Common iliac	9	17	26
Hypogastric	6	7	13
Uterine	17	20	37
Ovarian	19	22	41
Vaginal	4	5	9

TABLE III. INCIDENCE OF METASTATIC EMBOLI IN 70 PATIENTS WITH SUPPURATIVE PELVIC THROMBOPHLEBITIS

Pulmonary infarction	27
Cerebral abscess	1
Pulmonary abscess	4
Heart (subacute bacteriae endocarditis)	2
Mycotic aneurysm	1

TABLE IV. 169 BLOOD CULTURES IN 42 PATIENTS WITH SUPPURATIVE PELVIC THROMBOPHLEBITIS

Positive cultures	23
Patients with positive cultures	12

TABLE V. ORGANISMS RECOVERED IN 70 PATIENTS WITH SUPPURATIVE PELVIC THROMBOPHLEBITIS

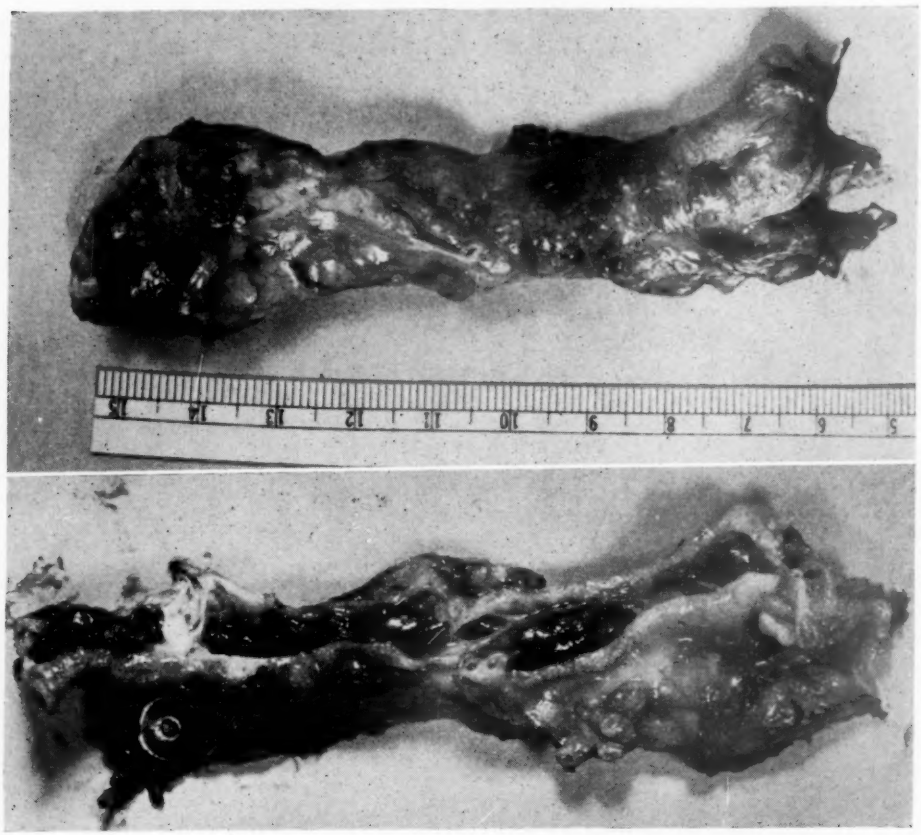
Staphylococcus albus	4
Staphylococcus aureus	4
Streptococcus, anaerobic	2
Streptococcus fecalis	1
Streptococcus β hemolyticus	1

TABLE VI. INITIATING FACTORS IN 70 PATIENTS WITH SUPPURATIVE PELVIC THROMBOPHLEBITIS

Vaginal delivery	26
Abortion	25
Cesarean section	5
Pelvic abdominal operation	4
Pelvic inflammatory disease	3
Uterine fibroids	3
Intracavitary radium	2
Perirectal abscess	1
Posttrauma	1
Total	70

both venous systems (Table I). Moreover, in all but 9 cases the clot was found below the level of the lower portion of the inferior vena cava in the veins draining directly into this vessel (Table II). In the 9 exceptions, the thrombotic involvement of the inferior vena cava usually extended only an inch or two above the confluence of the common iliac veins. As multiplicity of thrombi was the rule, these observations tend to support the rationale of ligating both the inferior vena cava and the ovarian vessels to prevent potentially lethal embolic complications.

A.



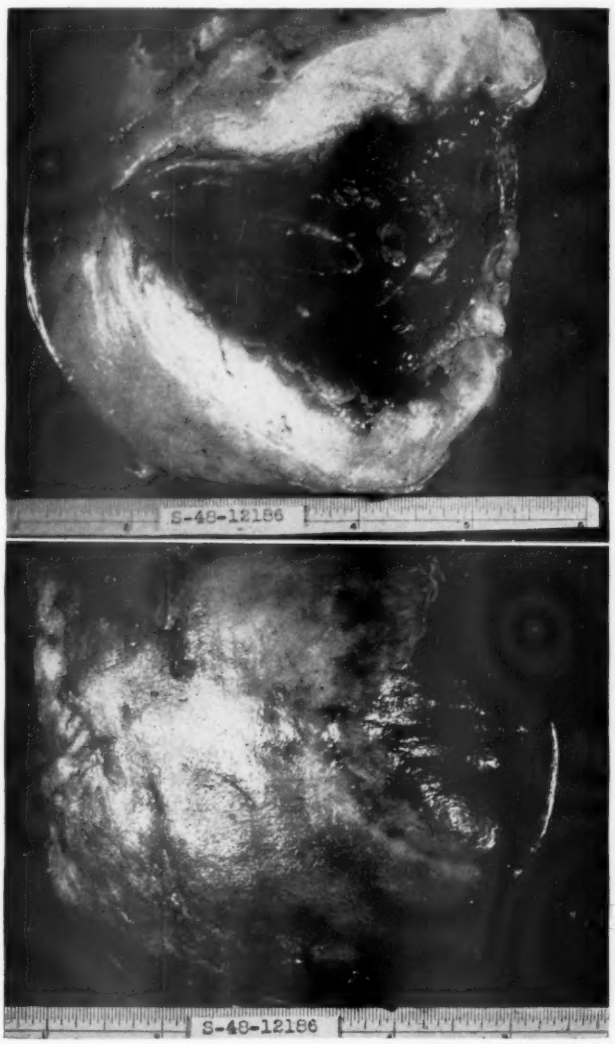
B.

Fig. 2.—*A*, Resected ovarian veins showing thrombi. Note the indurated edematous perivascular tissue. *B*, Veins opened to show large friable thrombi.

In the majority of cases portions of the resected ovarian vessels were available for examination (Figs. 2, *A* and *B*). Obviously, segments of other thrombotic pelvic veins were not removed as these patients were critically ill, and prolongation of surgical procedures to remove a portion of the iliac, hypogastric, uterine, or vaginal veins was not justified. The presence or absence of gross thrombi in these vessels, however, was corroborated at the time of laparotomy by at least two members of the surgical team in each case. In ad-

dition, specimens of Fallopian tubes and ovaries were available in the cases in which the degree of infection or gangrene indicated their removal. In 1 case gangrene of the uterus as a result of a circulatory disturbance fostered by the suppurative process necessitated hysterectomy (Figs. 3, *A* and *B*). Thus, the presence of suppurative pelvic thrombophlebitis could be detected histologically in the uterine sinuses, uterine veins, and ovarian veins.

A.

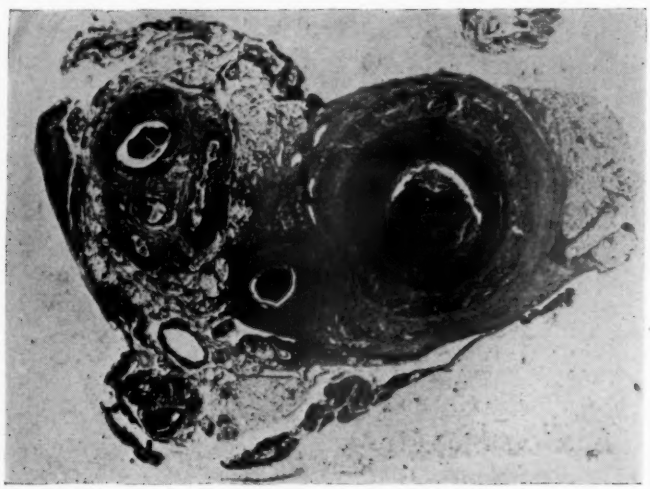


B.

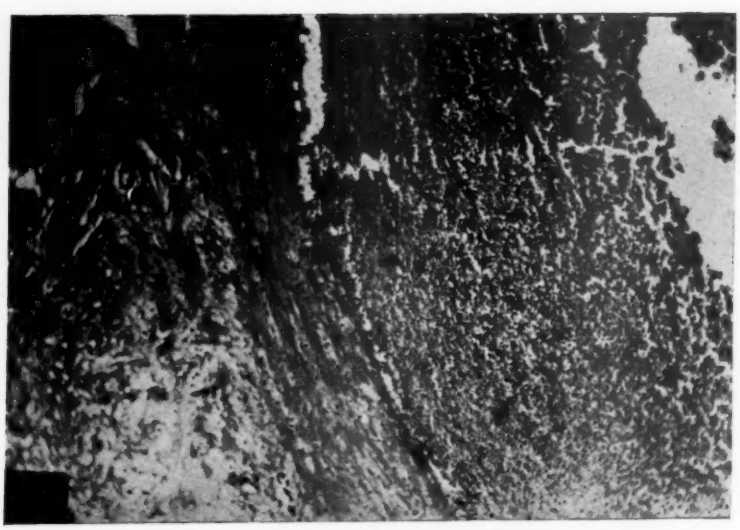
Fig. 3.—*A*, Uterus showing a large, gangrenous area in the fundus. *B*, Gangrenous uterus incised showing necrotic endometrium.

Grossly, thrombosis was accompanied by edema and induration, progressing to suppuration and actual areas of necrosis of the walls of the veins. These veins were palpably thickened, and friable clots could be felt in the lumen of the vein. In fulminating cases the normal sheen of the wall of the veins was replaced by

a yellowish cast. When the involved vein was opened, thrombotic material was friable and easily detached (Fig. 2, *B*). Thick, purulent accumulations with small particles of thrombotic material were rare. More often the material was seropurulent (Fig. 4, *A* and *B*).



A.



B.

Fig. 4,*A*.—Section of vein with septic thrombus (low power). *B*.—High-power section of the same area shown in 4,*A*. Note the inflammatory reaction in the intima and perivascular tissue.

Microscopically, the lesion was traced in the uterine sinuses in the 1 case of gangrene of the uterus (Fig. 5). In this case the thrombus was definitely septic with an admixture of polymorphonuclear leucocytes. Surrounding myometrium showed an acute inflammatory reaction with areas of necrosis. In the utero-ovarian anastomotic venous plexus, evidence of thrombosis was accom-

panied by varying microscopic pictures. Early thrombotic lesions were seen in the presence of an acute inflammatory response of the surrounding tissue. Although it was impossible to follow the steps in the development of thrombosis microscopically, it would seem as if perivascular inflammation, perhaps lymphatic in origin, caused the phlebitis, with endothelial damage resulting in the deposition of fibrin and the formation of a thrombus (Figs. 6 and 7).

Fig. 5.

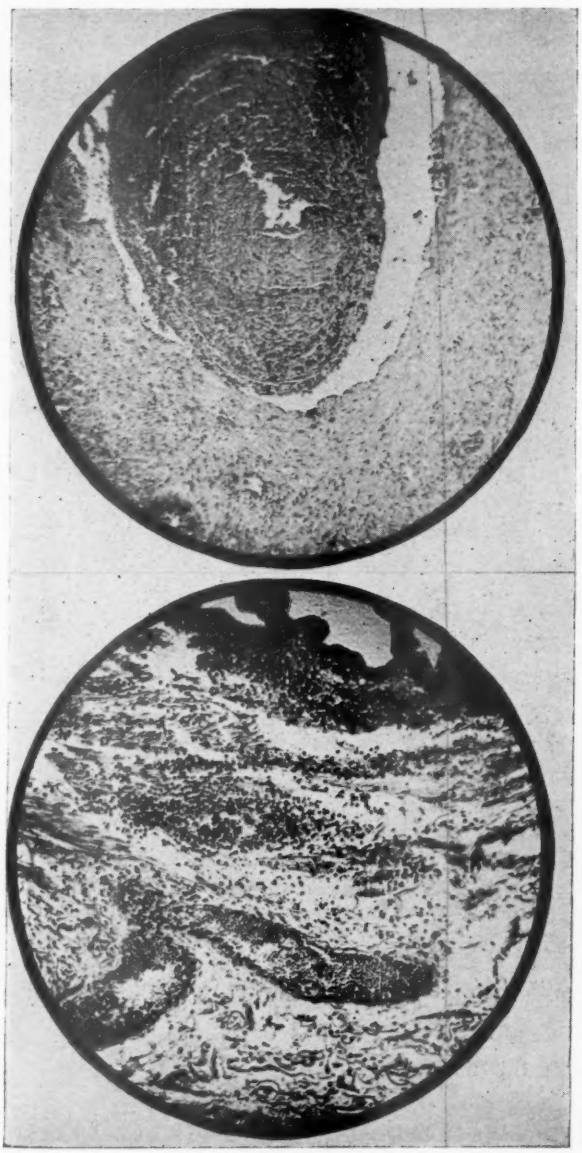


Fig. 6.

Fig. 5.—Septic thrombus in the uterine sinus. Note the large number of polymorphonuclear leucocytes.

Fig. 6.—Prounounced perivascular inflammatory reaction in the tubal wall. Note the venules with endothelial damage and fibrin deposition and the accumulation of blood elements in the earliest stage of clot formation.

Early lesions were similarly visible in the ovaries (Fig. 8). They contained, in the small venous radicles, hyaline-like clots composed almost solely of fibrin (Fig. 9). More advanced lesions were also in evidence in resected ovarian veins. Bacterial invasion of the actual clot was, in rare instances, evidenced by the presence of clouds of bacteria. More often, dense infiltration of acute inflammatory cells with subsequent degeneration indicated formation of frankly purulent areas in the thrombosed material (Fig. 4, *A* and *B*).

From the study of all pathologic specimens removed we believe that the pathologic sequence is intimal damage of the vein as a result of bacterial

Fig. 7.—Uterine section showing inflammatory cells in the thrombi in the uterine sinuses.

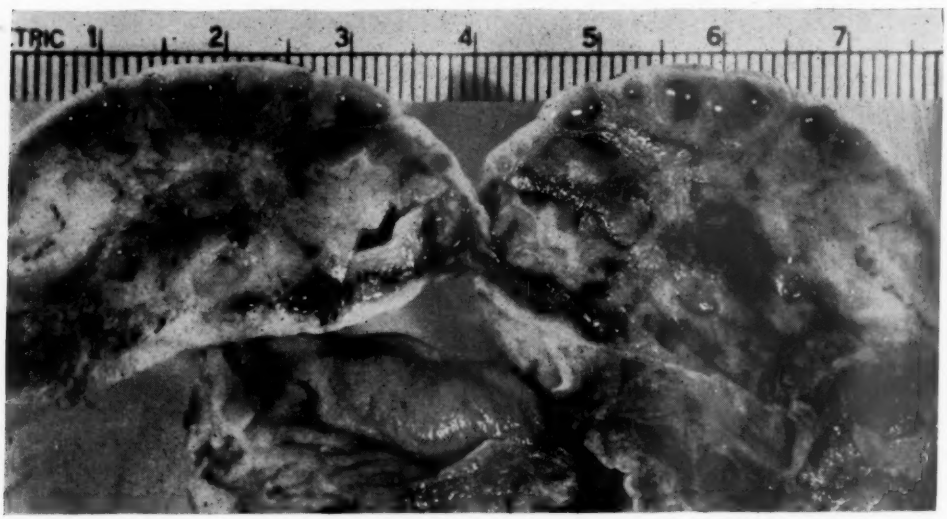


Fig. 8.—Gross specimen of resected ovary, revealing dark areas of infarction secondary to thrombosed venules.

invasion by direct extension along the intima or via the perivenous lymphatic channels. Following intimal damage, clotting processes are initiated. Subsequent bacterial invasion of the clot itself produces suppurative thrombophlebitis with liquefaction, fragmentation, and septic embolism.

We have attempted to show the development of this process in the preceding description of segments of tributaries of the ovarian veins and the ovarian vein itself. It is logical to assume that the same process occurs in the other large venous drainage systems from the uterus, that is, the uterine, hypogastric, and common iliac veins and the vena cava. We do not deny that post-partum clotting in the uterine sinuses at the placental site may be of the bland type at first and that later it may be invaded by bacteria, but we do contend that extension of the clotting process past the normal confines of the uterus in the vast majority of cases occurs in the manner just described.

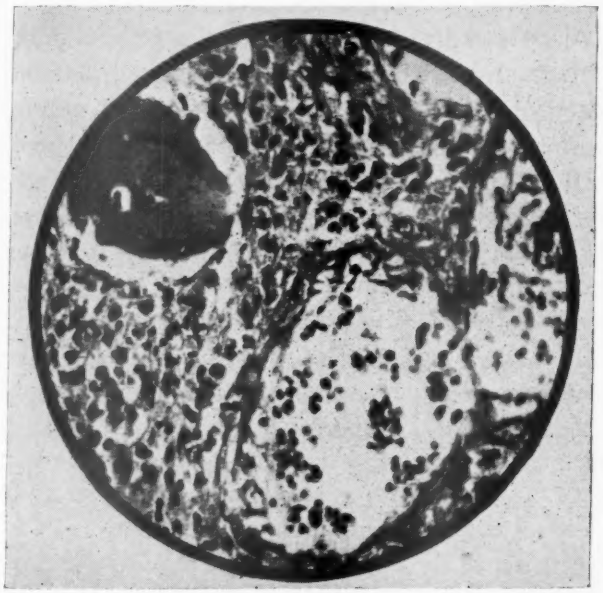


Fig. 9.—Microscopic section of a vein in the ovary shown in Fig. 8. Note the endothelial damage, perivascular inflammation, and beginning thrombus formation.

The importance of embolism is revealed in the incidence of pulmonary infarction in this series (Table III). Clinical evidence of embolism was found in 27 cases with roentgenographic confirmation in 24 of these. In 4 of the 27 cases the septic infarction progressed to actual abscesses, necessitating lobectomy in 2 instances and lobotomy in 1. In 2 cases implantation of the infected emboli on the cardiac valves resulted in subacute bacterial endocarditis, necessitating prolonged hospitalization and antibiotic therapy.

The formation of metastatic abscesses in other organs was an important cause of protracted illness in 3 additional cases. Cerebral abscess developed in 1. In this case it might be postulated that secondary metastasis occurred from the lungs through the vertebral veins or alternatively as a parodoxical embolism. The importance of metastatic abscesses is shown by a study of the

8 patients who succumbed despite the operative procedure. In the cases in which necropsy was performed, abscesses were found in the lungs, spleen, liver, kidney, brain, and heart, and in 1 patient a mycotic aneurysm was found. It is to be noted, however, in this connection that in no case was massive pulmonary infarction the cause of sudden death. Death resulted from pyemia and septicemia. Presumably, prevention of repeated infected embolisms would have permitted these patients to recover. Obviously, surgical therapy was applied too late to be of any avail.

ETIOLOGY

In studying the sites of thrombosis, we made an effort to determine the presence of thrombosis in the veins of the leg in order to ascertain if the latter played a role in the genesis of suppurative pelvic thrombophlebitis. In 12 of the 70 patients there was presumptive evidence of thrombosis in the veins of the leg as revealed by swelling and the presence of tender, thrombosed, cordlike veins in the leg. In 8 of these patients, although the thrombosis in the veins of the leg could have been the starting point of pelvic thrombosis, it is believed that the reverse situation occurred; that is, the thrombi had spread in a retrograde fashion from the veins of the pelvis to those of the leg. Bauer[10] believed that involvement of the veins of the leg might arise secondarily to pelvic thrombophlebitis, since 10 per cent of his cases of femoral iliac phlebitis were of pelvic origin. In the remaining 4 patients with large fibroids, whether the thrombophlebitis originated in the pelvis or leg is conjectural.

Since the embolizing potentialities of suppurative pelvic thrombophlebitis have been emphasized, studies of anaerobic and aerobic bacteriologic cultures of specimens of the peripheral blood were undertaken in 42 of the 70 patients. Of 169 cultures 23 yielded positive results, or results were positive in 12 patients (Table IV). These results are disappointing, but they reflect the difficulties of such a study. To obtain a positive reaction in an individual case often repeated cultures must be taken. Ideally, the blood sample should be taken during a "temperature spike" when embolism of the infected thrombus is occurring. Moreover, arterial puncture is said to be more efficacious than venous puncture. From this study the impression was also gained that whereas chemotherapeutic and antibiotic agents were given to most patients in massive doses preoperatively, these tended to render the peripheral blood sterile, but their action was not similarly effective in reaching the local pelvic infection. This impression is supported by only 1 case in this series in which culture of the venous blood was negative, whereas organisms were found on culturing thrombosed material from the resected ovarian veins. Although the importance of anaerobic streptococci in the genesis of puerperal infection has been demonstrated, these organisms did not seem to play a predominating role in this series (Table V). These results suggest that blood cultures may be diagnostically helpful if positive results are obtained, but they are of no value when negative and, as Neuhof and Seley[11] concluded from their study of suppurative phlebitis, they are of no aid prognostically.

In regard to the mode of entry of the infecting organisms, examination of Table VI shows the initiating factors in the 70 cases of suppurative pelvic thrombophlebitis. Full-term delivery, either vaginal or abdominal, preceded the majority of cases, and abortion, especially of the criminal type, was the next commonest factor. Pelvic operation, tubo-ovarian abscess, and trauma produced by intrauterine radium application also were active in the genesis of this disease. In short, infection of the surfaces of the genital tract from vulva to tubal ostium with associated trauma was the common denominator in all cases.

CONCLUSIONS

Suppurative pelvic thrombophlebitis is a distinct entity resulting from pelvic sepsis affecting the pelvic veins. The resulting purulent clots tend to break off in showers as small infected emboli. This can occur even though massive antibiotic and anticoagulant therapy is administered, and the result is development of metastatic abscess. Death is nearly always due to maintenance of a septicemic state by the original focus, secondary abscesses, or both.

Prevention of embolism and limitation of the spread of suppurative pelvic thrombophlebitis should permit the patient to recover by confining the infection to the pelvis. This can be accomplished by ligation of the inferior vena cava and ovarian veins, which should be done early enough to insure interruption of the normal venous return of the uterus proximal to the clotting process.

From a study of the material removed at the time of operation for suppurative pelvic thrombophlebitis complicating delivery or abortion, pelvic abscess, or radium application, we believe that infection of the wall of the vein causes deposition of fibrin on the infected intimal surface with the development of a thrombus which later tends to liquefy in the presence of bacterial invasion, resulting in an acute inflammatory reaction with local necrosis. The initial inflammatory involvement of the wall of the vein may result either from infection of the surrounding perivascular tissue or from extension along the length of the vein from a more distant location. Whatever the mechanism, intimal damage precedes the clotting process. Thrombi, while in the process of formation or when completely formed, are infected. This infection is manifested pathologically by lesions varying from mild polymorphonuclear infiltration to the presence of frank pus.

Suppurative pelvic thrombophlebitis is a condition not to be confused with phlebothrombosis or thrombophlebitis of the veins of the leg. In phlebothrombosis of the veins of the leg there is a bland clot with danger of fatal pulmonary embolism. In thrombophlebitis of the veins of the leg (phlegmasia alba dolens) an adherent, infected, but not often suppurative, clot is present. Minor aseptic pulmonary infarction occurs infrequently and lethal pulmonary embolism rarely. In suppurative pelvic thrombophlebitis infection most frequently precedes the clotting process with later suppurative and fragmentary tendencies, death resulting from multiple embolic abscesses or septicemia.

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SUPPURATIVE PELVIC THROMBOPHLEBITIS

II. Symptomatology and Diagnosis

A Study of 70 Patients Treated by Ligation of the Inferior Vena Cava and Ovarian Veins

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A PREVIOUS communication[1] presented a discussion of the etiology and pathology of suppurative pelvic thrombophlebitis based on an analysis of 70 cases encountered since July, 1941, in which ligation of the vena cava and both ovarian vessels was performed. The present paper is concerned with a discussion of the diagnosis and symptomatology of suppurative pelvic thrombophlebitis based on the same series of cases.

SYMPTOMATOLOGY

Chills and fever are the commonest clinical manifestations of suppurative pelvic thrombophlebitis. Chills occurred in 67 per cent of the 70 patients in this series. The patient was considered to have a chill only if it was noted by a person other than the patient, so that the term is used here as representing a true reaction to the bacteremia. Usually, chills result from septic emboli, but this cannot always be proved clinically. As reported in Part I of this study, the results of blood culture were positive in only 12 of 70 patients, and, though a positive result is occasionally of diagnostic aid, a negative result is of neither diagnostic nor prognostic value. The interval between the onset of the disease and the appearance of chills, fever, or both was not constant. In some patients chills were observed as early as the first post-partal day and in others as late as 3 weeks following delivery or abortion. In general, the more frequently chills occur, the more extensive and severe the phlebitic process. However, the number and frequency of chills prior to institution of surgical therapy have little or no influence on the mortality rate.

Pyrexia is usually pronounced. The course the temperature follows is generally of the "picket fence" variety (Fig. 1) with excursions that may range from normal to peaks of 106° F. These episodes of hyperpyrexia may be preceded by severe rigors. Ninety per cent of the patients in the present series had hyperpyrexia. Of the 3 puerperal patients in which the temperature did not rise above 101° F., 1 had proved pulmonary infarction, 1 chronic suppurative thrombophlebitis with repeated pulmonary infarction, and 1 retrograde

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thrombosis of the veins of the leg following cesarean section. All, however, had proved suppurative phlebitis of the pelvic veins at operation. Four patients were afebrile. Two of these had had a hysterectomy with prominent

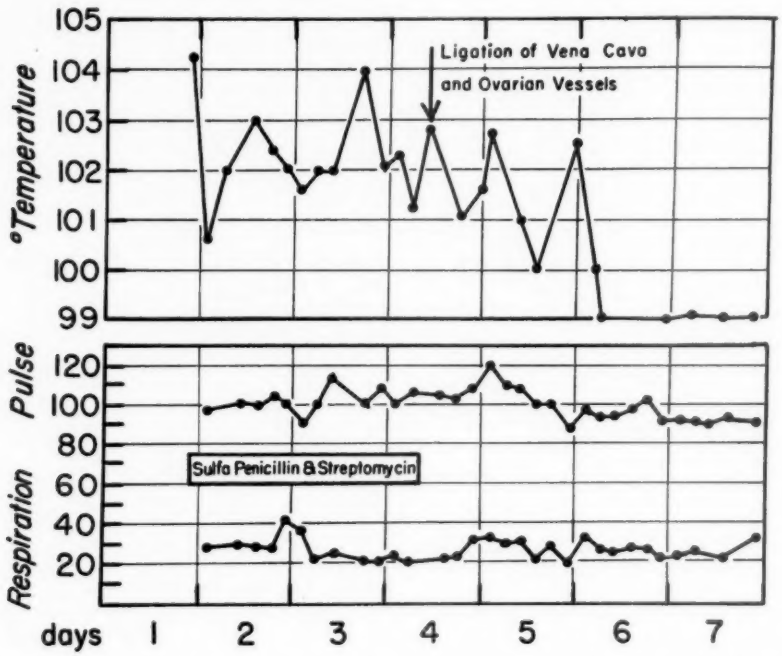

Fig. 1.—Graphic representation of the temperature, pulse rate, and respirations of a patient with suppurative pelvic thrombophlebitis showing "picket fence" type of temperature and sustained, elevated pulse rate.

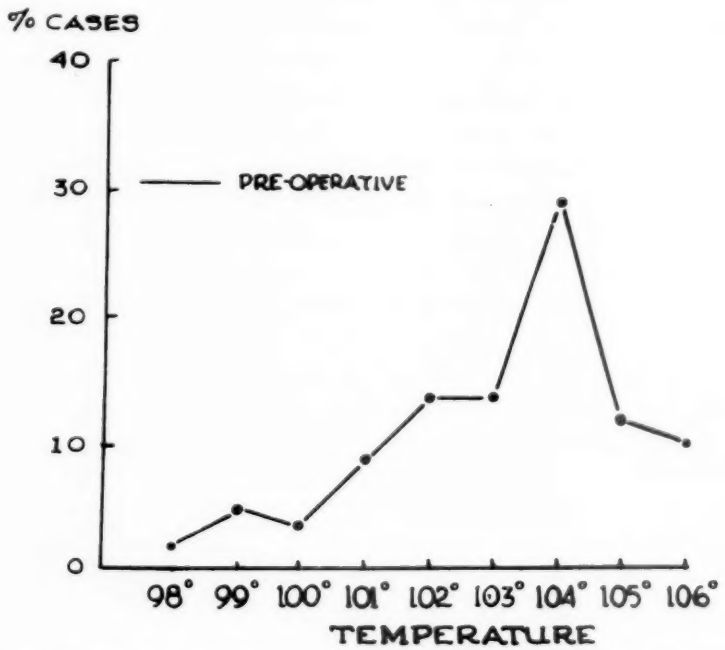

Fig. 2.—Composite graph of the temperature records of 70 patients with suppurative pelvic thrombophlebitis.

signs of venous clotting in the leg, 1 had massive iliofemoral thrombophlebitis complicating a large myoma of the uterus, and 1 had postoperative peritonitis with prominent signs of intravascular clotting in the leg and proved pul-

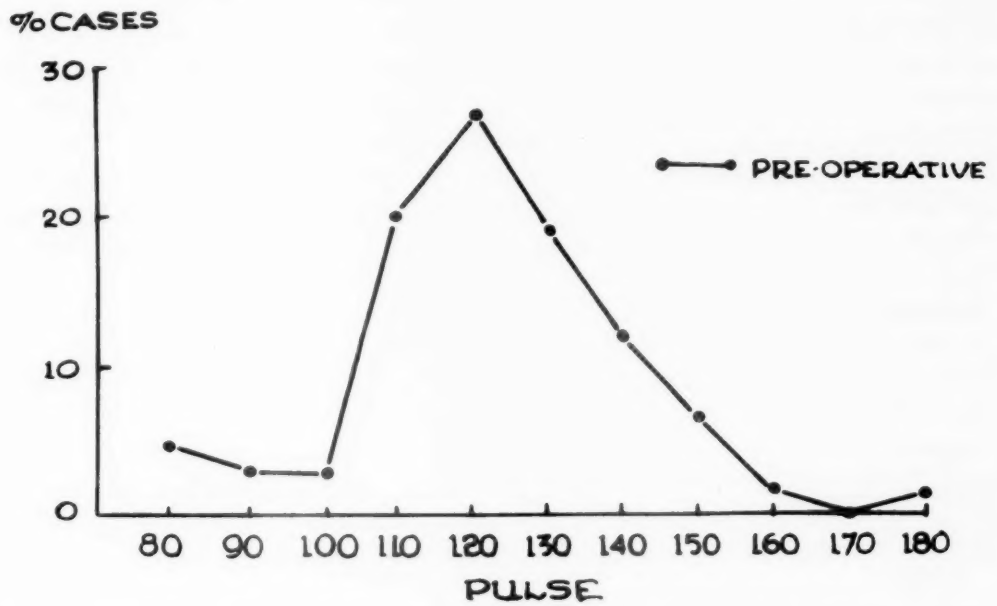

Fig. 3.—Composite graph of the pulse rates in 70 patients with suppurative pelvic thrombophlebitis.

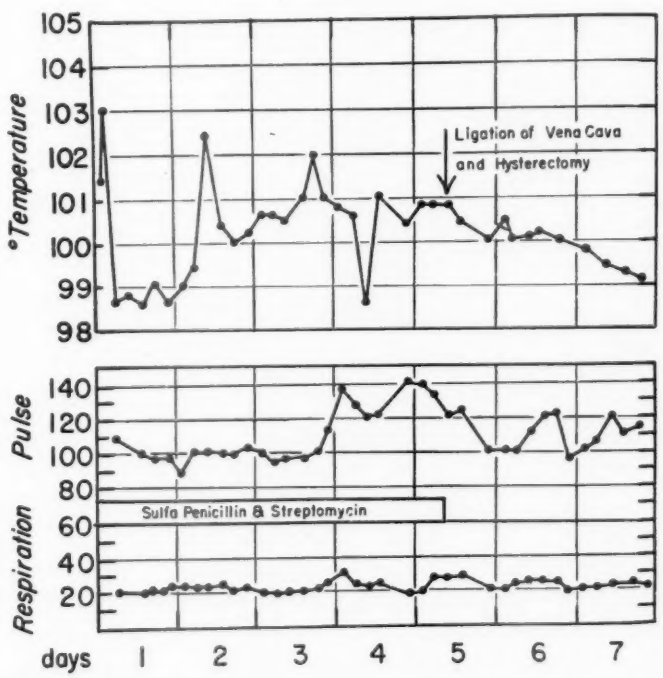

Fig. 4.—Graphic representation of a patient with suppurative pelvic thrombophlebitis. The temperature responded well to antibiotics. The temperature chart is of the plateau type. There was a pronounced increase in the pulse rate. Operation revealed gangrene of the uterus in addition to the thrombophlebitis.

monary infarction. In all, suppurative pelvic thrombophlebitis was found at the time of ligation of the inferior vena cava. Thus, the majority of patients with suppurative pelvic thrombophlebitis showed hyperpyrexia, but in a few, especially those with prominent leg signs (retrograde thrombi), pyrexia was mild or absent (Fig. 2).

Pulse.—The pulse rate is characteristically rapid and of a plateau type despite the wide excursions of the temperature. Eighty-nine per cent of the 70 patients in this series had a rapid, sustained pulse rate (Fig. 3). The pulse rate itself is not as important as the difference between the previous pulse rate and the elevated rate. For example, a patient with post-partal sepsis may be having fever spikes to 103° F. daily with a concomitant rise in pulse rate to

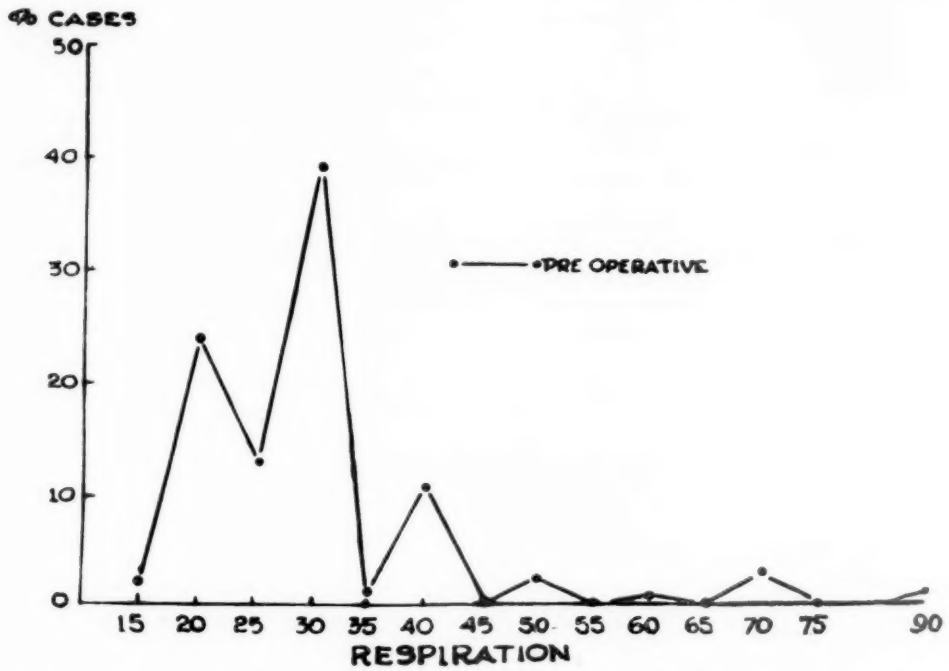

Fig. 5.—Composite graph of the respiratory rates in 70 patients with suppurative pelvic thrombophlebitis.

120 only to show a return to a rate of 80 when the temperature drops to 99 or 100° F. However, if the same patient continues to run a septic temperature, even though the temperature is only moderately elevated, and if the pulse rate rises to 100 or above and is sustained at that level despite drops in temperature, then the possibility of suppurative pelvic thrombophlebitis must be considered. A constant elevated pulse rate is as significant in the diagnosis of suppurative pelvic thrombophlebitis as in the diagnosis of phlebothrombosis or thrombophlebitis of the legs (Fig. 4).

Respiratory Rate.—An elevated respiratory rate is observed in most cases and does not necessarily indicate pulmonary involvement. An increased rate was observed in 83 per cent of the patients in this series (Fig. 5).

Pulmonary Manifestations.—It is important to recognize pulmonary signs and symptoms, not only because we consider evidence of infarction an indication for surgical treatment, but also because frequently infarction in suppurative pelvic thrombophlebitis presents no typical sign, symptom, or roentgenographic pattern. Often such cases are misdiagnosed as primary pulmonary diseases, such as pneumonia, pneumonitis, patchy atelectasis, miliary tuberculosis, pleurisy, or pulmonary abscess of unknown etiology. It is especially in this group of cases that failure to recognize the true primary lesion results in death or unfortunate sequelae. The classical wedge-shaped roentgenographic pattern is seldom seen, as the emboli are usually small, multiple, and infected. The fact that they are infected and small often results in local pneumonitis that may be demonstrated in any shape, size, or location, or even not at all until an abscess forms. On the other hand, a roentgenogram of the chest may sometimes reveal an area of infarction without other clinical manifestations. Therefore, it is our policy to have a roentgenogram of the chest made in all septic cases upon admission or when signs of sepsis develop and to repeat such studies until the patient is greatly improved or well. A single roentgenogram of the chest is not sufficient in these cases unless it demonstrates definite evidence of pulmonary infarction. We have observed patients with high fever, chills, and elevated pulse rates in whom there was no positive roentgenographic evidence of infarction until 48 to 72 hours following admission. Pulmonary shadows in the roentgenograms were found in 46 per cent of the patients in this series. It cannot be too frequently emphasized that any patient with a history of pelvic operation, pregnancy, thrombophlebitis, or pelvic trauma who complains of sudden thoracic pain must be thoroughly examined to exclude the possibility of embolism, however small, from the leg, pelvic veins, or both.

Thoracic pain, cough, hemoptysis, or any combination of these occurred in 37 per cent of the patients in this series. Clinical signs of infarction of the lungs were detected in 45.7 per cent. Clinical and roentgenographic correlation was not always possible in the same patient, but of the patients with infarction, both clinical and roentgenographic evidences were present in 93 per cent. Pleural effusion was not an outstanding sign. Moreover, in patients in whom it occurred and on whom pleural aspiration was performed, the characteristics of the aspirate did not aid in establishing a diagnosis of pulmonary infarction. This point is emphasized because some rely upon the presence of blood in the pleural fluid to substantiate the diagnosis of pulmonary infarction. In our experience the aspirated fluid has been more likely to be serous than bloody.

PELVIC EXAMINATION

Vaginal examination may reveal a thrombosed, tender vein or veins leading from an infected episiotomy wound or vaginal or cervical laceration. On the other hand, one may not be able to palpate any thrombosed veins either in the vagina or pelvis. Not infrequently, hard, tender cords may be felt in the base of the broad ligaments, or tender wormlike masses may be palpated in the fornices. In the majority of cases, however, palpable parametritis is not

evident, and the uterus is freely movable. Usually the character of the lochia is of no import. The uterus may or may not be enlarged to the size characteristic of the post-partum date on which the examination is performed. Only infrequently are an enlarged tender ovary, ovarian abscess, or cul-de-sac abscess encountered. In other words, the pelvis is usually normal to palpation except for the possible presence of tender thrombosed veins. The latter are usually not present if the thrombotic process has not extended past the myometrial veins or is most severe in the ovarian veins. Vigorous pelvic examination is usually followed by a pronounced rise in temperature. Thus, if no palpable evidence of thrombosis is found, the pelvis should be vigorously massaged and the subsequent temperature chart observed. A pronounced rise in temperature within 24 hours of this maneuver usually indicts the pelvic organs or vessels; conversely, failure of the temperature to rise usually eliminates the pelvic organs and veins as contributing to the patient's illness.

As stated previously, absence of palpable vaginal or pelvic veins on vaginal examination does not mean that suppurative pelvic thrombophlebitis is not present. Obviously, many pelvic veins are so situated anatomically that it is impossible to palpate them. Furthermore, extensive suppuration can exist in the venous sinuses of the uterus, serve as a focus for septic emboli, and not be palpable either vaginally or intra-abdominally. In the present series the site of thrombosis, as later confirmed at operation, was accurately predicted in 60 per cent of the patients. In the majority of the remaining patients thrombi were found in pelvic veins not accessible to vaginal, rectal, or abdominal palpation. In a few instances, at laparotomy thrombi were found in veins so located that they should have been palpated on physical and vaginal examination but were not. Occasionally, thrombi may not be detected on physical examination or at the time of operation, but ligation of the vena cava and ovarian vessels should still be performed. We have observed cases at autopsy wherein only the venous sinus of the uterus was involved in the suppurative process. The presence or absence of palpable veins in the leg, edema, tenderness in the calf, diminished pulsation in the dorsalis pedis arteries, or Homans' sign neither negate nor confirm the presence of suppurative pelvic thrombophlebitis.

DIAGNOSIS

The diagnosis of suppurative pelvic thrombophlebitis (puerperal pyemia) is often difficult to make because of the protean nature of the disease. For this reason many cases are unrecognized. Some patients recover following medical treatment, whereas in others the disease progresses unrecognized to complicated pathologic problems of the pelvis and other organs with resultant chronic invalidism or death. Constant awareness of this entity and its ramifications, timely recognition, and prompt and judicious application of medical and surgical therapy can lower the otherwise high morbidity and mortality rates.

History taking is of primary importance in the diagnosis of suppurative pelvic thrombophlebitis as in any disease. Often, as in cases of induced abor-

tion in which the patient is reluctant to admit pregnancy, much less interference, only by persistent questioning can the true story be obtained. Also, it is only by means of careful and complete history taking that the onset of acute or chronic sepsis can be definitely linked to a previous pregnancy of recent or remote occurrence. In questioning the patient, it is well for the physician to remember that suppurative pelvic thrombophlebitis can follow normal or operative obstetrics. Moreover, it often develops after induced abortion and, occasionally, as a complication of pelvic or perirectal abscess or following intrauterine application of radium. Trauma, anemia, toxemia, prolonged labor, and hemorrhage are all predisposing factors.[1, 2] Thus, the length and course of labor, method and site of delivery, type of anesthetic, presence or absence of toxemia and hemorrhage, and previous therapy should be recorded in detail. Usually, in acute cases signs of sepsis develop any time from 1 day to 6 weeks following termination of pregnancy. All too often the patient with fever, chills, or both is admitted to some hospital service other than gynecology or obstetrics, the true focus is overlooked, and long and even fatal delay may result before the true nature of the disease is recognized. By constant awareness of the fact that fever, chills, or both might be the result of suppuration in the vessels, many women who otherwise might die can be saved. The fact that a palpable abscess of the cul-de-sac, tube, or ovary is not present does not mean that a pelvic condition is not the cause of the septic symptoms. Severe suppurative pelvic thrombophlebitis can exist without any palpatory signs.

Since suppurative pelvic thrombophlebitis is an infectious process, the differential diagnosis is broad. In the cases we have observed, sickle-cell crisis in the pregnant or puerperal Negro has presented a diagnostic problem. The clinical picture is one of severe sepsis. We believe that in every Negro woman having chills, fever, or both, an extensive hematologic survey should be made in order to rule out the diagnosis of sickle-cell crisis. Lupus erythematosus, complicated by or following pregnancy, can present the same features. These two diseases are mentioned specifically because on any large obstetric or gynecologic service they will be encountered not infrequently. Other infectious diseases, such as malaria, typhoid fever, pulmonary tuberculosis, meningitis, acute infectious disease, and pyelonephritis, are readily differentiated.

The diagnosis is made by awareness of the possibility of the presence of this disease, knowledge of the pathologic picture, close observation of the daily temperature, pulse rate, and respiratory rate, and repeated examination of the chest, including roentgenography, for evidence of pulmonary infarction. Familiarity with the technique of palpation of thrombosed pelvic veins is of particular value. Constant alertness as to the possibility of the existence of suppurative thrombosis of the pelvic veins facilitates recognition of the disease at a time when application of therapy is most effective.

CONCLUSIONS

1. The diagnosis of suppurative pelvic thrombophlebitis is often difficult to make. Only by careful questioning concerning previous pregnancies and

constant awareness of the possibility of the presence of this disease can diagnostic errors be reduced.

2. The triad of symptoms—chills, fever, and increased pulse rate—in any puerperal woman demands inclusion of suppurative pelvic thrombophlebitis in the differential diagnosis.

3. Repeated examination of the chest, including roentgenography, is mandatory. In the present series roentgenograms of the chest revealed pulmonary shadows in 46 per cent of the patients. In some cases there were no clinical signs or symptoms of infarction, but the roentgenograms of the chest were diagnostic.

4. Careful pelvic examination will reveal thrombosed vaginal or pelvic veins in 60 per cent of the cases. However, the absence of palpable thrombosed pelvic veins in no way means that suppurative pelvic thrombophlebitis does not exist.

5. The presence or absence of signs and symptoms of thrombosis of the veins of the legs does not rule out suppurative pelvic thrombophlebitis.

6. Suppurative pelvic thrombophlebitis is a distinct pathologic entity. The mortality and morbidity rates from this disease can be greatly reduced by prompt recognition and judicious application of therapy.

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SUPPURATIVE PELVIC THROMBOPHLEBITIS

III. Surgical Technique

A Study of 70 Patients Treated by Ligation of the Inferior Vena Cava and Ovarian Veins

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SINCE 1941, we have been utilizing surgical therapy in cases of suppurative pelvic thrombophlebitis that prove refractory to medical regimen.[1, 2] Despite the now general use of sulfonamides and antibiotics, we still see a number of patients with postabortal or post-partal sepsis in whom the primary focus is in the pelvic veins, suppurative thrombi occurring in the inferior vena cava, common iliac, external iliac, hypogastric, uterine, or ovarian veins, or a combination of one or more of these. We believe that best results in these cases proving refractory to medical regimen are obtained by ligation of the venous returns from the uterus, that is, the vena cava and both sets of ovarian vessels. It is the purpose of this paper to describe the technique of this procedure.

INDICATIONS

It is interesting that our indications for ligation are the same today as they were in 1941. These include (1) any patient having postabortal or post-partal sepsis who fails to respond to medical regimen in 4 or 5 days, (2) any patient with postabortal or post-partal sepsis in whom a pulmonary infarct develops while being treated conservatively, or (3) any patient admitted to our service with post-partal sepsis and infarction.

APPROACH

Ligation of the vena cava and ovarian veins may be performed through an extraperitoneal or transperitoneal approach. In patients who have previously had a hysterectomy, the continuity of the ovarian vessels with the uterus has already been interrupted so that, in such cases, the extraperitoneal approach to the vena cava may be employed. However, in post-partal or postabortal sepsis or suppurative pelvic thrombophlebitis arising as a result of a pelvic abscess or intrauterine application of radium, the transabdominal approach is necessary for 2 reasons. First, it is easier in this manner to ligate the venous channels from the uterus, that is, the vena cava and both right and left ovarian vessels, and, second, not infrequently the phlebitic process is extremely severe in the ovarian vessels and can extend as high as the left renal vein just below the entrance of the right renal vein to the vena cava.

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PREOPERATIVE PREPARATION

All patients with suppurative pelvic thrombophlebitis are acutely ill. This is especially true of the ones in whom the thrombotic process is a complication of delivery or abortion and in whom medical regimen has been unsuccessful. Since a transabdominal approach is indicated in these cases, decompression of the bowel by Wangensteen suction for 12 to 24 hours preoperatively will facilitate performance of the procedure. It has been our practice to employ Wangensteen suction in any patient who is obviously not improving under medical regimen and probably will require surgical therapy. Moreover, in patients requiring immediate operation decompression of the intestine is begun promptly, and, although the amount of decompression of the intestine is not as great as if it had been employed for 24 hours preoperatively, it does lessen the difficulty from dilated intestinal coils. As for any operation, blood is readily available for transfusion if necessary.

TRANSABDOMINAL APPROACH

Anesthesia.—Spinal anesthesia is preferable for the transabdominal approach. Many of these patients have associated pulmonary disease, and we believe that ultimate oxygenation is better achieved than with general or intravenous anesthesia. Furthermore, spinal anesthesia allows for dilatation of the blood vessels in the extremities which are in spasm if the thrombosis involves any of the major veins of the extremities or pelvis. It has been our experience that some internists and anesthetists who have not seen many of these patients operated on are reluctant to favor spinal anesthesia because the patients are so ill. Despite objections from internists or anesthetists, the surgeon should insist on a spinal anesthetic. Most of the patients in the present series had a spinal anesthetic with no untoward reactions. In the few cases in which a general anesthetic was used, performance of the surgical procedure was made more difficult.

Technique.—After the desired level of anesthesia has been obtained, the patient is placed in the supine position and an infusion started with a large gauge needle into one of the veins of the arm. Following preparation of the abdomen, an incision is made from just above the symphysis pubis upward to about 5 cm. above and to the right of the umbilicus (Fig. 1). The rectus fascia is incised and the right rectus muscle retracted laterally. The posterior layer of the rectus fascia and the peritoneum are then incised. The vascular channels of the pelvis and the ovarian veins are palpated and the location of thrombotic areas identified. If thrombotic veins are not found, it is still necessary to carry out the procedure as planned, since it is not always possible to palpate the course of all the veins deep in the pelvis or the small thrombi frequently found in the microscopic section of the walls of the uterus, pampiniform plexus, or ovaries.

The cecum and ascending colon are retracted medially, and a longitudinal incision is made into the posterior peritoneum approximately along the line of fusion of the visceral and parietal peritoneum (Fig. 1). The cecum and

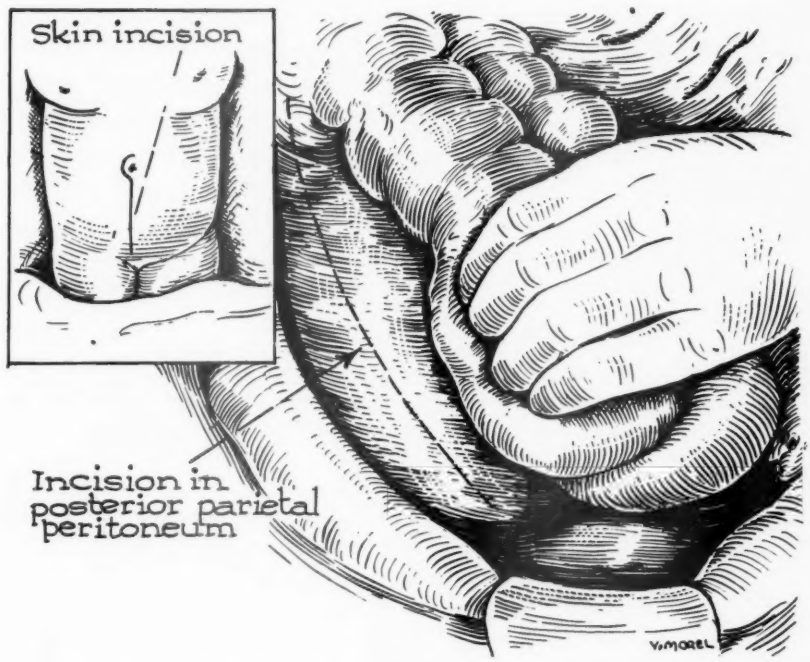


Fig. 1.—Transabdominal approach for ligation of the vena cava and ovarian veins and mobilization of the cecum and ascending colon.

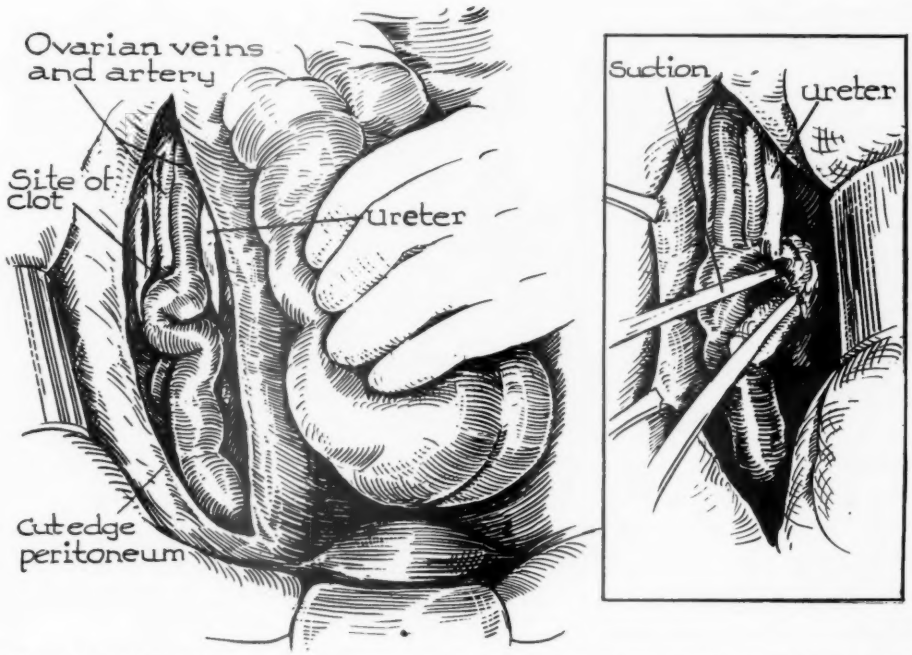
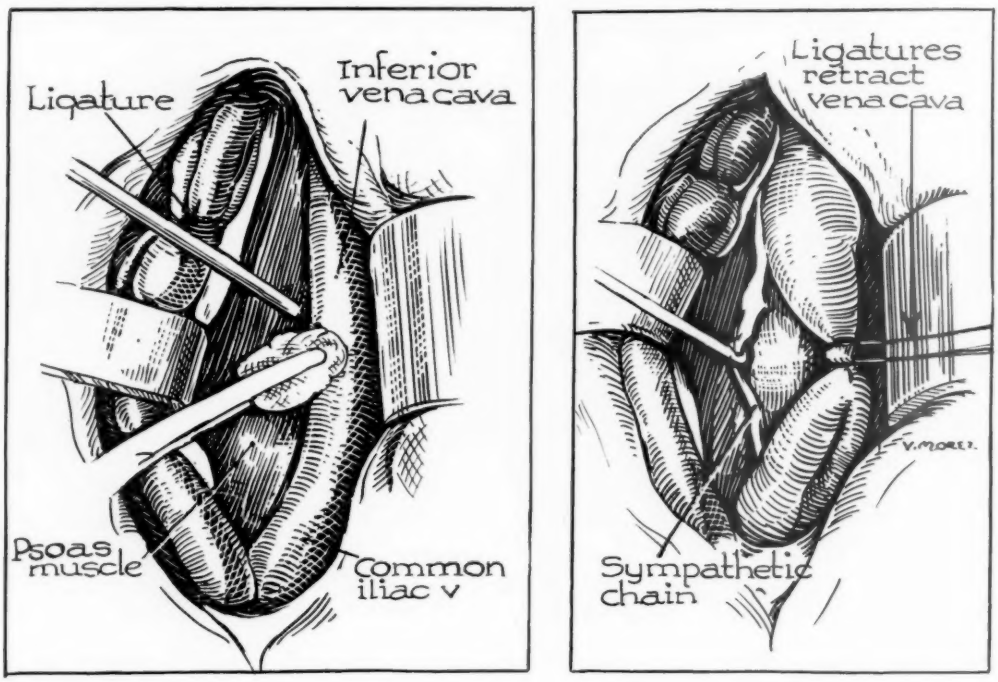


Fig. 2.—Mobilization of the cecum and ascending colon medially, exposure of the retroperitoneal area, and identification of the right ovarian vessels and ureter. Inset shows the method of dissecting the ureter from the ovarian vessels.

lower portion of the ascending colon are then mobilized to the midline, and the retroperitoneal area is exposed. The right ovarian vessels and right ureter are identified. In some cases in which the phlebitic process in the ovarian vessels is severe, identification of the ureter may be difficult. However, its positive identification is mandatory before the ovarian vessels are ligated, since it may easily be ligated in error. Traction on the tube and ovary caudalward facilitates identification of the ovarian vessels, as in this manner they are drawn taut. Also stimulation of the ureter by stroking with a hemostat will reveal peristalsis which, of course, is not noted in the ovarian vessels. The ureter is separated by blunt dissection from the ovarian vessels by means of a suction tip and "dissector." The latter is composed of a small roll of umbilical tape gripped firmly between the jaws of a large, curved Kelly clamp (Fig. 2).



A. *B.*

Fig. 3.—*A*, The ovarian vessels have been ligated proximal to the thrombus. The vena cava is dissected from the surrounding tissue. *B*, The ovarian vessels and ureter are retracted laterally. The ligated vena cava is retracted medially. The sympathetic chain is identified.

After the right ovarian vessel has been identified, a ligature of quilting cotton No. 40 is placed around both artery and veins proximal to any thrombus found (Fig. 3, *A*). If no thrombus is found in the right ovarian vessels, it is mandatory to ligate them anyway. Quilting cotton No. 40 is utilized as the ligature. Section of the vessels is not necessary unless a portion is to be removed for pathologic study.

Following ligation of the right ovarian vessels, the retroperitoneal space is further exposed medially until the inferior vena cava is identified. The inferior vena cava is found by the junction of the common iliac veins at a level

corresponding to the intervertebral disc between the third and fourth lumbar vertebrae. It is unusual to find variance in the formation of the vena cava. If the inferior vena cava is not easily identified because of pericaval cellulitis, its positive identification can be assured by tracing the common iliac vein on the right side to its junction with the left iliac vein.

By means of a suction tip and "dissector" the inferior vena cava is gently freed from the surrounding tissue. Frequently, large lymph nodes can be seen immediately anterior to the inferior vena cava; in freeing these from the inferior vena cava, some bleeding may result from the blood vessels of the lymph node. This can be easily controlled by pressure and clamping; ligature suturing is not necessary. Should one of the lumbar veins be torn during the dissection, immediate pressure over the area will control the bleeding until a hemostat can be applied to the vessel. If torn, the lumbar vein should be ligated with quilting cotton No. 40 or occluded by a small silver clip.

Once the inferior vena cava has been isolated from the surrounding tissue for a distance of 2 or 3 cm., a ligature of crochet cotton No. 10 or 20 is passed around it by means of a ligature carrier or aneurysm needle. Another ligature of the same material is applied about 1 cm. proximal or distal to the first, and both are tied.

The site of ligation may be anywhere between the formation of the inferior vena cava and the lower level of the right renal vein, depending upon the extent of thrombus formation in the inferior vena cava or site of exposure If no thrombus is found in the iliac veins or inferior vena cava, the inferior vena cava should nevertheless be ligated. We do not believe it necessary to divide the inferior vena cava. In the few instances in which this has been done, no differences were noted in the extremities of the patients as compared with those in whom ligation was in continuity.

Ligation of the inferior vena cava above the level of the right renal veins is disastrous. Should a thrombus be found extending proximal to the junction of the left renal vein the cava should be incised, the thrombus removed by suction, and the inferior vena cava ligated just distal to the confluence of the right renal vein and cava.

The right lumbar sympathetic chain is then identified (Fig. 3, *B*) and severed. After hemostasis is assured, the ascending colon and cecum are replaced, and the incised margins of the parietal peritoneum are approximated.

The left ovarian vessels are then identified in the infundibulopelvic ligament. If any thrombi are noted, the ovarian vessels are ligated above the thrombus. Should the thrombus extend above the infundibulopelvic ligament, the descending colon is mobilized medially, the left ovarian vessels and ureter are identified, and the ligature is placed above the thrombus. In some of our patients the thrombus extended to the left renal vein. The technique is the same as that for ligation of the right ovarian vessels. If the ascending colon has to be mobilized because of the extent of the thrombus, the right lumbar sympathetic chain is identified and cut. As ligation of any major vessel supplying or draining an extremity is accompanied by vasospasm, it is important

that when the vena cava is ligated the sympathetic nerve supply to the extremity or extremities be interrupted by cutting the main sympathetic nerve or nerves supplying the area at the time of ligation or by procaine blocks postoperatively. Even if no thrombotic process is seen in the left ovarian vessels, they are ligated nevertheless (Fig. 4). Success in combating the phlebitic process depends upon ligation of the venous returns from the uterus, that is, the inferior vena cava and right and left ovarian veins. The abdominal incision is then closed with interrupted sutures of quilting cotton No. 40.

EXTRAPERITONEAL APPROACH

An extraperitoneal approach is used in those patients in whom the thrombotic process originated in the veins of the leg or in those with thrombosis of the pelvic veins in whom the ovarian channels have already been interrupted, that is, as after hysterectomy. We believe that the combination of lumbar sympathectomy with vena cava ligation has helped considerably in the rehabilitation of our patients.

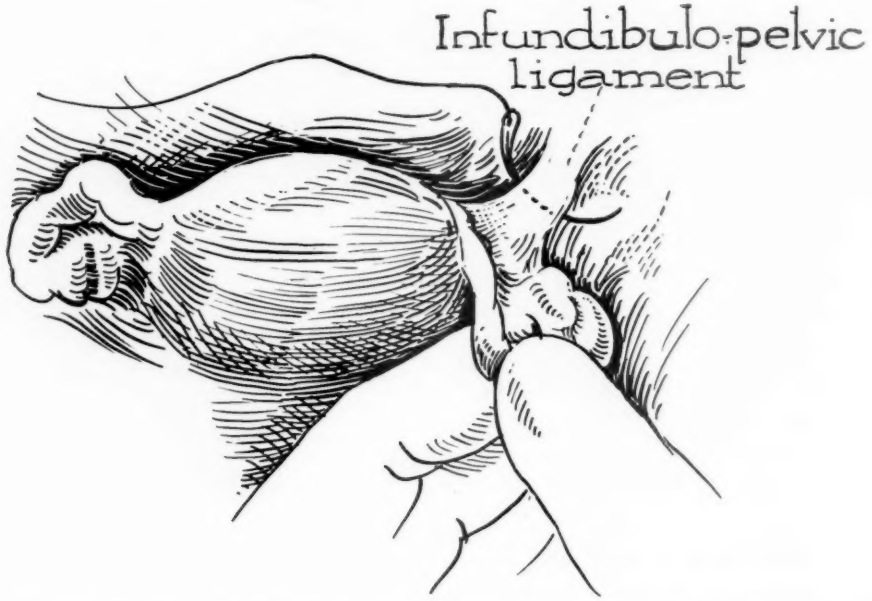


Fig. 4.—The left ovarian vein is ligated. If the thrombus extends higher, there is mobilization of the descending colon and sigmoid colon medially.

Technique.—The patient is placed in the supine position on the operating table, titled slightly to the left side (particularly in obese individuals). The skin of the entire abdomen is prepared and an area so draped as to expose the abdomen from the costal margin superiorly to the pubis inferiorly and from flank to flank.

A curved Leriche incision[3, 4] with the convexity laterally is then made on the right side of the abdomen, lateral to the right rectus muscle mass (Fig. 5, *A*). The incision is carried down through the external oblique fascia and muscle in the same plane as the cutaneous incision. The internal oblique and

transversus abdominis muscles are then split in the direction of their fibers, this incision being made about 1 handbreadth (10 cm.) above the right anterosuperior iliac spinous process (Fig. 5, *B* and *C*). This latter measurement obviously will have to vary slightly, depending upon the body build of the patient. The method, however, is accurate enough so that the incision through the internal oblique and transversus abdominis muscles is placed at this level opposite the body of the third lumbar vertebra. If placed any lower, the anomalies of the level of the formation of the vena cava can mislead the operator, and the right common iliac vein may be ligated in the belief that it is the vena cava.

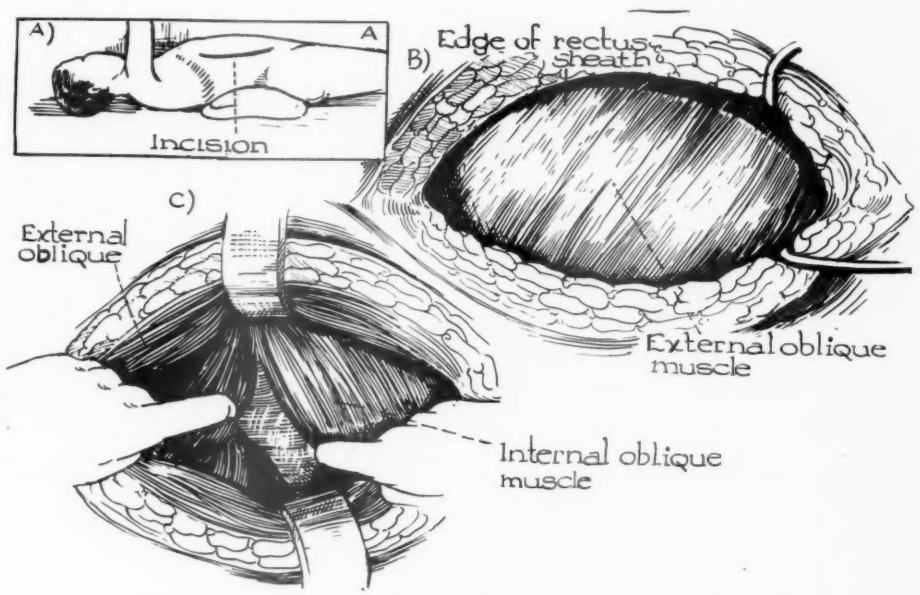


Fig. 5.—Extraperitoneal approach for ligation of the vena cava and ovarian veins. *A*, Position of the patient. The patient's arm is not necessarily elevated but may be fastened at the side. The Leriche incision is employed. *B*, Incision through the external oblique muscle. *C*, Splitting of the internal oblique muscle.

After the muscle-splitting incision is made through the internal oblique and transversus abdominis muscles, the edges of this incision are retracted superiorly and inferiorly to expose the retroperitoneal tissues. The reason for the curved Leriche incision through the skin, subcutaneous tissue, and external oblique muscle and fascia instead of a simple transverse incision now becomes apparent, for it allows much wider retraction of the deeper, transverse muscle-splitting incision and thus much wider exposure of the retroperitoneal space.

The retroperitoneal tissues and transversalis fascia and peritoneum are then swept medially by blunt dissection along the curve of the internal surface of the transversus abdominis muscle until the edge of the psoas muscle is met. This dissection is begun laterally to avoid opening the peritoneum. It is then carried up over the anterior surface of the psoas muscle. Care must be exercised when the lateral border of the psoas muscle is first encountered, as the

dissection can inadvertently be carried posteriorly to this muscle instead of anteriorly. This error exposes the lumbar plexus of nerves and leads to confusion in orientation and extreme difficulty in retraction and exposure of the vena cava. Continuing over the anterior surface of the psoas muscle, the surgeon identifies the genitofemoral nerve lying on the anterior surface and descending laterad. On the medial border of this muscle and lying on the anterior surfaces of the bodies of the lumbar vertebrae will be seen the dark blue inferior vena cava. The peritoneum is then retracted by means of a Deaver retractor and a large pack (Fig. 6, *A*).

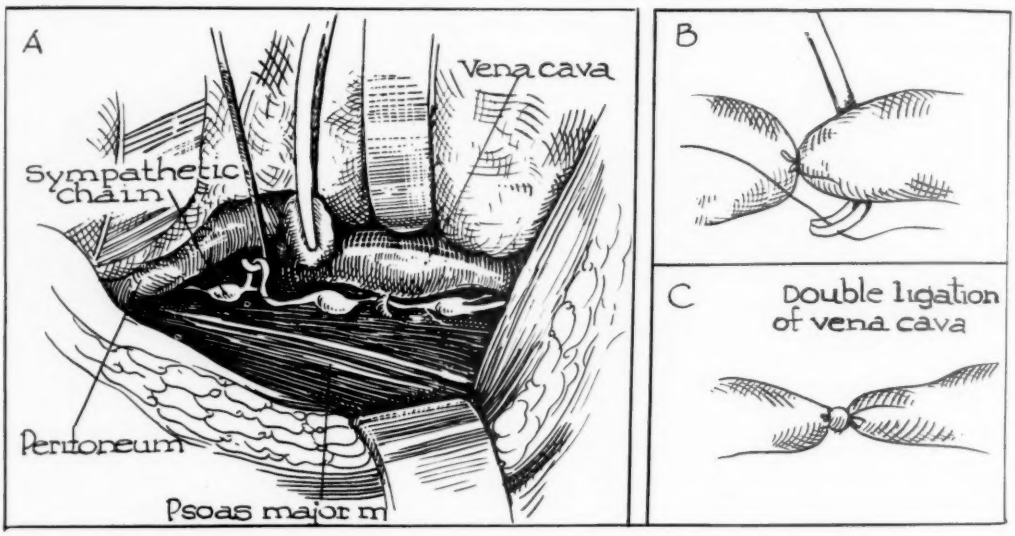


Fig. 6.—*A*, Exposure of the retroperitoneal space and identification of the vena cava, sympathetic chain, and psoas muscle (with genitofemoral nerve lying on it); *B* and *C*, ligation of the vena cava in continuity.

In patients with sparse retroperitoneal fat, the ureter will be seen in this fat, having been carried medially and anteriorly with the peritoneum. In women, the ovarian vein will be a more or less prominent vessel, lying in the retroperitoneal fat, lateral to the ureter. This vessel can dilate to enormous size if the iliac veins are occluded, and the inferior vena cava may be temporarily mistaken for it. In men the spermatic vein may occasionally be identified.

The fourth lumbar vein is usually a prominent and constant vessel coming off the vena cava and going posteriorly behind the psoas muscle at the level of the inferior border of the fourth lumbar vertebra. Gentle, blunt dissection around the vena cava just above this point will usually isolate this vessel just above its formation. In a few instances, further dissection will be necessary in a cephalad direction in order to identify the confluence of the iliac veins. This point should always be positively identified in order to insure ligation of the vena cava itself and not the right common iliac vein alone, as pointed out before.

After isolation and elevation of the vena cava, the vessel is ligated in continuity with No. 10 or 20 crochet cotton ligatures (Fig. 6 *B* and *C*). The vessel is not divided unless palpation prior to ligation raises the question of extension of a thrombus cephalad within the vena cava. In such cases, the vena cava is opened between the ligatures, which are used as stays, the thrombus removed by suction proximally, and the vessel then ligated. The ligatures are then reinforced with suture ligatures of the same material, both on the proximal and distal ends of the divided vena cava.

Sympathectomy.—The lumbar sympathetic chain on the right side is identified usually lying on the anterolateral aspects of the vertebral bodies between the medial border of the psoas muscle and the vena cava. At times, the psoas muscle may have to be retracted laterally in order to identify the chain, as it sometimes lies beneath this muscle, and at other times it may be beneath the vena cava. Variations in position, size, and shape of the chain are common. This makes careful exploration of the anterior surfaces of the vertebrae mandatory so as not to miss aberrant fibers or possibly one-half of a double chain. Inspection may be misleading, and search for the chain may seem to be fruitless; in such cases palpation may sometimes reveal the chain. The most constant ganglion, according to Cowley and Yeager,[5] occurs on the second lumbar vertebra, usually at its lower one-third. Our experience also has been that the upper first and second ganglions are most easily identifiable; since the chain is usually larger in its upper portion, identification at this upper level is easier. The occasional communicating branches to the opposite lumbar chain must also, of course, be identified and removed. The chain must not be confused with the genitofemoral nerve lying on the anterior surface of the psoas muscle and, unlike the chain, descending in a lateral direction.

The chain is elevated on nerve hooks and extirpated by avulsion above the first lumbar ganglion and at or just below the level of the fourth lumbar ganglion. Avulsion above the first ganglion always raises the question of sterility in male patients by interfering with ejaculation. However, this complication actually has occurred rarely in our experience, and higher avulsion of the chain provides better denervation of the leg.

The retroperitoneal tissues may then be allowed to fall back into place after all bleeding has been controlled. It will be noted that small aberrant and inconstant lumbar veins may be torn in removing the sympathetic chain. This makes identification of the chain more difficult, but such bleeding is always easily controlled with pressure or small bits of Gelfoam and causes no trouble afterward. Individual ligation of these vessels is impossible because they are so short.

The incision is closed in layers with interupted No. 40 cotton sutures in all fascial planes overlying the muscles and No. 80 or No. 120 cotton sutures in the subcutaneous fascia and skin. A light dressing is applied to the wound. If the patient's condition permits, a lumbar sympathectomy is then done on the left side through an identical approach in the left flank.

POSTOPERATIVE CARE

In the majority of our patients the administration of antibiotics has been discontinued at the time of operation. If both sympathetic chains have been cut, lumbar sympathetic blocks are not necessary. If the sympathetic chains have not been interrupted, daily lumbar sympathetic blocks are performed for 4 or 5 days postoperatively. If only 1 sympathetic chain has been interrupted at operation (usually the right), then lumbar sympathetic blocks are performed on the uninterrupted side for 4 or 5 days. In the majority of our patients the veins in the leg proper were not involved and their valves were undamaged; therefore, elastic stockings were not recommended except when ligation of the inferior vena cava was performed for phlebothrombosis or thrombophlebitis of the leg veins. The patient is ambulatory within 24 to 48 hours of operation, and, except for utilization of lumbar sympathetic blocks, postoperative care is no different from that following any laparotomy on our service.

SUMMARY

Ligation of the inferior vena cava and ovarian veins is indicated in cases of suppurative pelvic thrombophlebitis that prove refractory to medical treatment. The procedure is performed through an extraperitoneal approach if the patient has previously had a hysterectomy since the continuity of the ovarian vessels with the uterus has already been interupted. The transabdominal approach is employed in all other cases. The technique of each approach is described in detail.

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TUMORS OF CHILDHOOD: SURGEON'S VIEWPOINT

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AMERICAN Cancer Society statistics for Oregon (1946) show that childhood cancer was responsible for more deaths in this age group than heart disease, tuberculosis, poliomyelitis, or congenital malformations. It was exceeded as a cause of death only by accidents. The magnitude of the problem was further emphasized to us when we made a preliminary survey of the tumor census of the Doernbecher Memorial Hospital for Children. During a three-year period from 1946 to 1949, 175 tumor cases were admitted, representing more than 2.5 per cent of the total number of hospital admissions. The distribution of cases in this series is indicated in Table I.

The Doernbecher Memorial Hospital for Children is a sixty-two bed unit of the University of Oregon Medical School Hospitals and Clinics. Operating as a state hospital, with an average of 2,200 hospital admissions annually, it serves a large geographical area. In recent years it has been the policy for every ward patient presenting a benign or malignant tumor to be referred to the general tumor clinic for diagnosis and recommendations as to therapy. Definitive operative procedures are then carried out by the various staff surgeons assigned to the Doernbecher Memorial Hospital.

On the basis of our experience with this tumor clinic group, we have been led to a consideration of the surgeon's viewpoint in regard to the tumors of childhood. Certain general conclusions would seem justified at this time:

1. The high death rate from the proved malignancies of childhood and the demonstration in recent years that the operative risk from major surgical procedures is not excessive suggest that a more radical approach to the treatment of the malignancies of childhood is warranted.

2. Whether utilizing surgical techniques or cancerocidal x-radiation, such an aggressive policy in therapy must, necessarily, be based on a unanimity of opinion as to the histologic diagnosis of malignancy.

3. The clinically malignant nature of some benign tumors and the possibility of malignant change in others indicate the advisability of prophylactic removal and histologic study of every tumor mass in the infant or child.

The illustrative case histories which will be presented are from the files of the Tumor Clinic of the University of Oregon Medical School Hospitals and Clinics. These cases have been recorded with the Children's Tumor Registry.*

CRITERIA OF OPERABILITY

Recent advances in the treatment of cancer are marked by two general trends: a revision of the surgeon's philosophy in the direction of more radical

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*The Children's Tumor Registry, Memorial Hospital for Cancer and Allied Diseases, New York, N. Y.

TABLE I. PEDIATRIC TUMOR CASE ADMISSIONS, DOERNBECHER MEMORIAL HOSPITAL FOR CHILDREN, JULY 1, 1946, TO JULY 1, 1949

LOCATION OF TUMORS	NUMBER OF CASES	
Vascular		59
Cavernous hemangioma, hemangioendothelioma	55	
Lymphangioma, cystic hygroma	4	
Lymphatic and Blood-forming Organs		30
Leucemia	18	
Lymphomas (Hodgkin's disease, lymphosarcoma)	7	
Reticuloendothelioses	5	
Brain, Nerve, and Related Structures		27
Neuroblastoma	6	
Medulloblastoma	3	
Craniopharyngioma	3	
Astrocytoma	2	
Neurogenic sarcoma	2	
Neurofibroma	2	
Ganglioneuroma	2	
Ependymoma	1	
Pheochromocytoma	1	
Miscellaneous	5	
Bone and Cartilage		13
Osteogenic sarcoma	2	
Ewing's tumor	2	
Chondroma	5	
Miscellaneous	4	
Skin and Related Tissues		17
Juvenile melanoma	1	
Large nevus	2	
Lipoma	4	
Miscellaneous	10	
Eye and Orbit		8
Retinoblastoma	5	
Melanoma	3	
Kidney		5
Wilms' tumor	5	
Larynx and Rectum		6
Papilloma	3 each	
Ovary		3
Dysgerminoma	1	
Adenocarcinoma	1	
Malignant teratoma	1	
Miscellaneous		7
Teratoma	2	
Malignancy, primary site not determined	5	
Total number of cases		175

attempts at cure, and intensification of the study of various endocrinologic and biochemical approaches to the problem.[19] Once the histologic diagnosis of malignancy is established (and this is a most important and difficult point in the case of childhood tumors) and the metastatic survey has been made, four basic considerations will determine the operability of the individual patient: (1) the biologic characteristics of the tumor; (2) the surgeon's philosophy and his technical ability; (3) the basic principles of cancer surgery; (4) the calculated risk of the operation.

If less than all of the neoplastic tissue is removed, the operation does too little. The effective surgical techniques for diagnosed malignancy are extensive procedures, not conservative or compromise operations. This approach to therapy has been stated by Brunschwig,[3] the exponent of ultraradical cancer surgery, as follows: "It is contrary to the basic principle in cancer surgery

to refrain, after exposure, from wide excision of a malignant neoplasm when this can apparently be carried out in so far as macroscopic evidence indicates that the neoplasm can be encompassed."

The opponents of this concept have attacked it by stating that the chance for cure is slight, the operative risk is excessive, and the destruction of tissue and mutilation of the patient contraindicate extensive surgical procedures in the treatment of advanced malignant disease. On the basis of sentiment and prejudice, even more resistance to radical surgery is encountered when the patient is an infant or child. Although the virulence of the malignancies of childhood is attested by a high death rate, the argument that all malignant diseases are incurable is not tenable. Cures have been reported in the treatment of cancer of almost every form and site. There are embryonic tumors, such as the neuroblastoma, which may even cease spontaneously to be malignant.[5] There is well-documented evidence[7, 15, 16] that early and proper treatment of childhood tumors may now be said to carry an increasingly good prognosis.

The general surgeon should be encouraged to press the operative attack by the admonition of an acknowledged leader in the field of cancer therapy. Pack[17] stated, "The good surgeon must worry whether his definition of inoperability is in his state of mind or moral courage, or in the actual stage of the cancer."

The tolerance of infants and children for extensive operative procedures has been demonstrated by the remarkable advances in the surgical treatment of congenital abnormalities. The Blalock operation for pulmonary stenosis, the division of the patent ductus arteriosus, the resection of a coarcted segment of the thoracic aorta, the operative cure of tracheo-esophageal fistula in the newborn infant, and many other examples can be cited. From the standpoint of the infant or child, even as in the adult patient with a cancer, the extreme end point of operability might be defined as "the extent of physiological strain that is within recoverable limits." In considering this point, Brunschwig[4] has made the following analysis: "The experience of those surgeons interested in very radical surgery for cancer would seem to indicate that, at the present time, the exact limits of operability are scarcely definable in anatomical terms unless structures would be removed that are physiologically indispensable to life, aside from any question of the extent of a neoplasm. Operability is defined at present in terms of the patient's ability to survive an extensive procedure that might produce marked physiological aberrations."

Normal anatomic structures are expendable in the surgical attempt to effect a cancer cure. It may be necessary to accept a destructive and mutilating procedure if this course is unavoidable. The techniques of reconstructive surgery can be utilized in the rehabilitation of the patient, but this consideration should not compromise the plan of surgical attack at the time the malignancy is removed. Radical surgery, when it can be done, is the cancer patient's best hope for cure. This approach to the pediatric tumor problem is illustrated by the following case report.

CASE 1 (175-816).—Osteogenic sarcoma of the femur; hip disarticulation amputation after bone biopsy.

A 13-year-old boy sustained an injury to the right leg four months before hospital admission. He developed a 6 by 3 by 2 cm. painful swelling just above the right knee, with radiographic evidence of a destructive process involving the femur. The metastatic survey was negative. A diagnosis of osteogenic sarcoma was established by biopsy. Four days later, hip disarticulation amputation (Fig. 1) was done. The postoperative course was uncomplicated.

He is alive and well with no evidence of metastases more than 18 months after the amputation. The boy is psychologically well adjusted to the loss of an extremity and the fitting of a prosthesis has been completed.

A radical mutilating surgical operation was accepted as necessary without hesitation on the part of the parents after biopsy had established an absolute histologic diagnosis of malignancy.

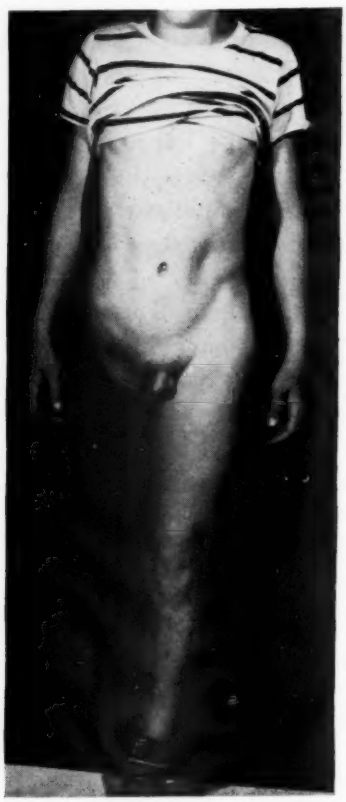


Fig. 1 (Case 1).—Hip disarticulation amputation for osteogenic sarcoma of the femur.

The biological characteristics of the tumors of childhood are unpredictable in many instances. A categorical denial of surgical treatment or x-radiation therapy by introduction of such terms as "biologically inoperable" and "radioresistant" is seldom possible in these cases, and would seem to constitute a challengeable and restrictive approach to therapy. In our tumor clinic group, at least, there is a definite trend toward a liberalization of the indications for cancerocidal x-radiation therapy in the treatment of certain pediatric tumor patients. The considerations which have influenced us to revise our concepts of x-radiation along more radical lines are: the embryonal and undifferen-

tiated character of many of the malignancies of childhood, the frequent disparity between histology and clinical course, the high percentage of radiosensitive tumors (regardless of the predictability of this on the basis of histologic study), and our experience with unexpected long-time survivals and apparent cures of inoperable or incompletely removed malignancies that have been treated by x-radiation. This explanation is the basis for our opinion that all of the malignant tumors of childhood which are not operable or resectable deserve a trial of therapy by x-radiation. There is reason to hope for a higher salvage rate if such a course is followed. The local tissue tolerance and general resistance of children to carefully fractionated x-radiation would seem to be favorable, even at cancerocidal doses. It is true that our experience with long-time follow-up studies of such cases is limited, but we have not yet encountered adnexal or squamous carcinomas of the skin in the field of irradiation in patients who have been followed for three to seven years after therapy.

The general indications, at the present time, for radiation therapy in the treatment of the malignancies of childhood are listed in Table II.

TABLE II. RELATIVE SUSCEPTIBILITY OF PEDIATRIC TUMORS TO X-RADIATION THERAPY

Lesions Treated by Radiation
Lymphomas
Lymphosarcoma
Lymphoepithelioma
Hodgkin's disease
Chronic lymphatic leucemia (spray x-radiation or P^{32})
Carcinomas of oro- and nasopharynx
Medulloblastoma (x-radiation of entire neural axis)
Histologically diagnosed malignancies which are inoperable or not resectable
Lesions Treated by Combined Surgery and Radiation
Bilateral retinoblastoma (enucleation of one eye, radiation to the other)
Teratoma of the testis (orchiectomy and postoperative radiation)
Seminoma of the testicle (orchiectomy and radiation to retroperitoneal nodes)
Postoperative radiation
Dysgerminoma of the ovary
Neuroblastoma
Wilms' tumor of the kidney
Ewing's tumor of bone
Lesions Not Treated by Radiation
Melanoma
Astrocytoma (unless inoperable or not resectable)
Acute lymphatic leucemia (Aminopterin therapy)

CRITERIA OF MALIGNANCY

Dargeon[6] would consider all tumors of childhood as malignant or potentially malignant. There is some value to a classification of pediatric tumors on the basis of clinical evidence of malignancy. The important practical consideration in diagnosis is not whether a condition can be labeled as either benign or malignant, but whether a favorable prognosis can be given to the parents.[13] It may be no more than an academic distinction to classify as benign a neoplasm, such as hemangioendothelioma, which shows a disturbing rapidity of growth, a tendency to recurrence following excision, local invasion of vital structures by the accident of its location, or even death from exsanguinating hemorrhage. Case II illustrates such a so-called "benign" tumor.

CASE 2 (166-126).—Multiple cavernous hemangiomas of subcutaneous tissues and intestinal tract, recurrent exsanguinating intestinal hemorrhages.

A 3-year-old girl was admitted to the hospital in December, 1947, because of multiple subcutaneous vascular tumors, severe anemia, and a history of repeated episodes of intestinal bleeding. At the age of 6 months, twenty-four subcutaneous hemangiomas had been excised.

Two subcutaneous hemangiomas were excised and she was given multiple blood transfusions for the anemia. Five months later, exploratory laparotomy was done because of severe recurrent intestinal bleeding. Five cavernous hemangiomas within the bowel wall were excised. The spleen and liver were normal in appearance. Two more laparotomies were done in June, 1948, and February, 1949, for the same indications. At the last follow-up visit, there had been no further exsanguinating intestinal hemorrhages. Numerous subcutaneous hemangiomas remain.

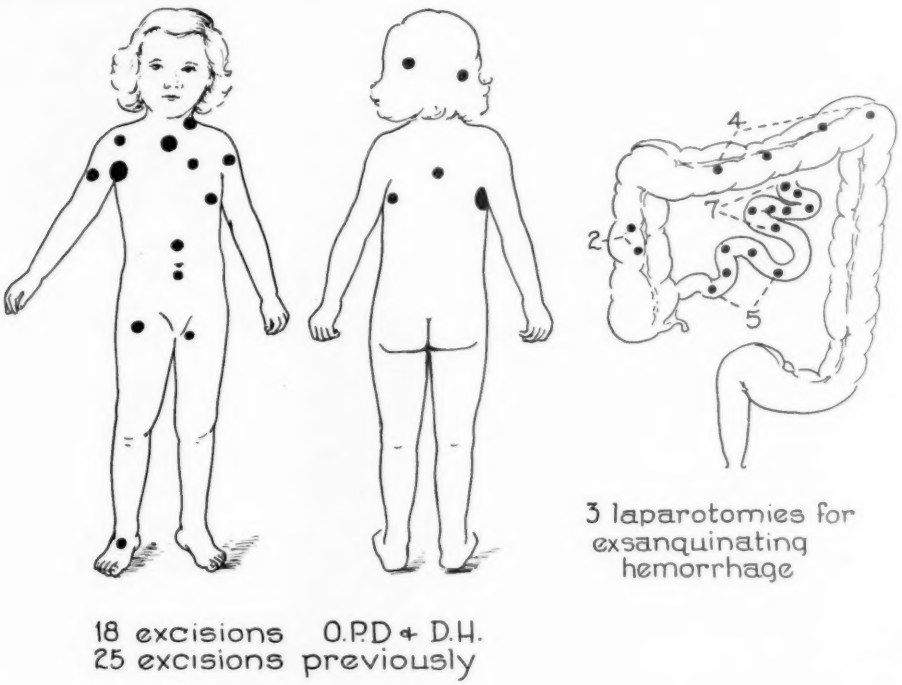


Fig. 2 (Case 2).—Diagram of the location of multiple subcutaneous and intestinal cavernous hemangiomas which have been surgically removed: a histologically benign-clinically malignant tumor.

It is for cases such as this, which manifest a high degree of clinical malignancy in spite of the benignancy of the histologic picture, that we suggest the clinicopathologic classification, histologically benign—clinically malignant.* Case 3 is an interesting example of the same type.

CASE 3 (173-942).—Sustained hypertension due to pheochromocytoma; preoperative use of adrenolytic compounds Dibenamine and Benzodioxane as diagnostic aids; clinical cure and near normotensive state following surgical removal of adrenal tumor.

A 13-year-old boy was admitted to the hospital in November, 1948, for diagnostic studies because of sustained hypertension, nocturnal sweating, occasional pain in the lumbar

*Malignant—Virulent, and tending to go from bad to worse (Dorland, W. A. N: The American Illustrated Medical Dictionary, Ed. 21).

region, headache precipitated by exercise, and loss of visual acuity. The blood pressure was 200/140 with correspondingly elevated femoral arterial pressures. There were hypertensive vascular changes evident on funduscopic examination, with edema of the discs and striate hemorrhages. There was no evidence of impaired renal function. The dextrose tolerance test was abnormal, the curve was of the diabetic type.

With the patient in the supine position, testing doses of Dibenamine produced a drop in blood pressure to normotensive levels. A similar response was elicited by the intravenous injection of Benzodioxane. The preoperative diagnosis was pheochromocytoma. At operation, a smooth, encapsulated, 28 Gm. tumor was removed from the adrenal region through a left flank incision. There was an immediate drop in blood pressure to near normotensive levels. The postoperative course was uncomplicated.

Follow-up studies in July, 1949, using Dibenamine, Benzodioxane, and histamine as testing drugs revealed, in each instance, a resting blood pressure of approximately 132/88. There was little or no response to the injections. The patient is asymptomatic and the retinopathy shows a definite reversal. A report of this case has been made by Pitcairn and Youmans.[18]

The most obvious grouping of the tumors of childhood would be into the two major categories, histologically benign—clinically benign and histologically malignant—clinically malignant. If the classification were to be carried to completion, other categories would be needed. For example, there are those unusual instances where a tumor may actually be histologically malignant—clinically benign. The two outstanding examples of this type are the juvenile melanoma and the rare neuroblastoma which disappears without treatment, or undergoes spontaneous change into a more differentiated and benign type of tumor.

Unfortunately, a further division of pediatric tumor cases is needed. There is, at the present time, a significantly large debatable or undiagnosable group of neoplasms in which a definite histologic diagnosis is impossible. A small part of our experience with this relatively large group of pediatric tumors is indicated in Table III. It is evident that the pathologist's dilemma becomes the surgeon's dilemma: there is the twofold problem of choice of therapy and statement of a prognosis. The two case reports which follow illustrate the difficulties that may arise.

CASE 4 (174-459).—Chronic cervical lymphadenopathy, biopsy followed by radical neck dissection, debatable histologic diagnoses, malignancy indicated by clinical course.

A 7-year-old boy developed a massive conglomerate lymphadenopathy over a period of three years involving the entire right side of the neck. There was no evidence of acute or chronic infection, hepatomegaly, splenomegaly, involvement of other nodal groups, or a primary source for metastatic malignancy that could be demonstrated by careful otolaryngologic study. There were no abnormalities of bone. Hematologic studies were negative, the purified protein derivative test and serology were negative. Lymph node biopsy was done in December, 1948, and this was followed by radical neck dissection. A 5 by 4 by 2 cm. mass was removed. Cultures for acid-fast organisms and guinea pig inoculation studies were negative.

There was no agreement as to the histologic diagnosis. Suggested diagnoses ranged from "no diagnosis, clinical course will have to determine it" to "reactive hyperplasia," "lymphosarcoma," Hodgkin's disease," "caseo-calcareous tuberculosis," and "chronic histoplasmosis."

TABLE III. PEDIATRIC TUMOR CASES; TABULATION OF MOST CONTROVERSIAL HISTOLOGIC DIAGNOSES (DOERNBECHER MEMORIAL HOSPITAL FOR CHILDREN, 1949)

CASE NO.	CONSULTING PATHOLOGIST AND DIAGNOSES									
	UNIVERSITY OF OREGON GROUP	A	B	C	D	E	F	G	H	I
187-199	Neurogenic sarcoma Sarcoma, type undifferentiated	Benign plexiform neuroma	Sclerosing angioma	Low-grade fibrosarcoma		Abscess and fibrosis			Lymphangioma	
170-638	Carcinoma simplex, branchial cleft or salivary gland Anaplastic carcinoma	Embryonal rhabdomyosarcoma		Malignant tumor, possible lymphosarcoma	No diagnosis		Lymphangioendothelioma Undifferentiated round-cell, tumor, malignant nonpigmented melanoma Mucous carcinoma, salivary gland	•	Salivary gland malignancy Endothelial sarcoma (Ewing)	
175-592	Undifferentiated carcinoma, highly malignant Neuroblastoma Adrenal tumor	Embryonal rhabdomyosarcoma	Angioendothelioma		Chordoma		Undifferentiated sarcoma		Meningeal sarcoma Endothelial sarcoma	
174-459	Reactive hyperplasia Hodgkin's disease	No diagnosis	Lymphosarcoma, small-cell type	Lymphosarcoma	Hodgkin's paragranuloma	Lymphosarcoma Histoplasmosis Tuberculosis	Hodgkin's disease			

175-444	Osteogenic sarcoma, telangiectatic type	Benign bone angioma or vascular giant cell tumor	Chondrosarcoma	Osteogenic sarcoma			Osteogenic sarcoma		Benign osteochondroma		
175-816	Osteogenic saroma	Osteogenic sarcoma									Lymphoblastoma
175-171	Granulomatous process Boeck's sarcoid	Negative node									
175-029	Neuroblastoma	Neuroblastoma	Lymphosarcoma	Metastatic sympathicoblastoma	Rhabdomyosarcoma	No diagnosis	Neuroblastoma				
182-360	Lymphoendothelioma	Lymphosarcoma	Lymphosarcoma	Lymphosarcoma		Reticulum sarcoma				Reticulum sarcoma	
166-126	Cavernous hemangioendothelioma Hemangioendotheliosarcoma	Cavernous hemangioma		Metastasizing hemangioma	Hemangioblastoma			Cavernous hemangioma			

University of Oregon group consists of eight to ten medical school and clinical staff pathologists.

Five months later, with the development of a satellite adenopathy at the periphery of the field of the radical neck dissection, x-radiation therapy was started. He is still under treatment.

Loss of time through observation of the debatable tumor that manifests its malignancy late may be a tragedy. On the contrary, the possible consequences of a diagnostic error that would label as malignant a benign lesion are suggested by Case 5.

CASE 5 (175-444).—Destructive telangiectatic tumor of bone involving the superior ramus of the pubis, histologic diagnosis of osteogenic sarcoma; treatment refused, histologic diagnosis now in doubt.

Fig. 3 (Case 5).—Roentgenogram showing destruction of the superior ramus of the left pubic bone. Histologic diagnosis uncertain after bone biopsy.

Three months before hospital admission, an 11-year-old girl sustained a fall, followed by severe pain in the left lower extremity with the development of a limp. Radiographic studies revealed destruction of the superior ramus of the left pubis (Fig. 3) with medial deviation of the bladder and left ureter by extrinsic pressure. A biopsy was done and a histologic diagnosis was made of osteogenic sarcoma, telangiectatic type, relatively low-grade malignancy. A large, firm mass could be palpated by abdominal and rectal examination in the area involved. Blood calcium and phosphorus levels were not abnormal; the alkaline phosphatase level was 16 King-Armstrong units. The metastatic survey was negative.

Further treatment was refused by the parents of the child and she was taken from the hospital. Permission for follow-up studies has been refused, but a roentgenogram of the pelvis was obtained seven months after she had been released from the hospital. There was no increase in size of the tumor mass and there was some evidence of recalcification in the area.

She is still alive sixteen months after bone biopsy. The final outcome of this case is unsettled. The histologic diagnosis of osteogenic sarcoma has been questioned by a consulting board of pathologists. The possibility exists that the biopsy is from a benign tumor of bone.[2]

Considerations such as these, and the awareness that we are only at the beginning of knowledge in understanding the tumors of childhood, provide *raison d'être* for the Children's Tumor Registry. The collected data and experience of many groups will be needed to correlate and reconcile the bizarre clinical course of some tumors, the instances of debatable or uninterpretable histologic evidence, the discrepancy which may exist between histologic characteristics of a tumor and its biologic growth tendencies, and the unexplained survivals in some cases.

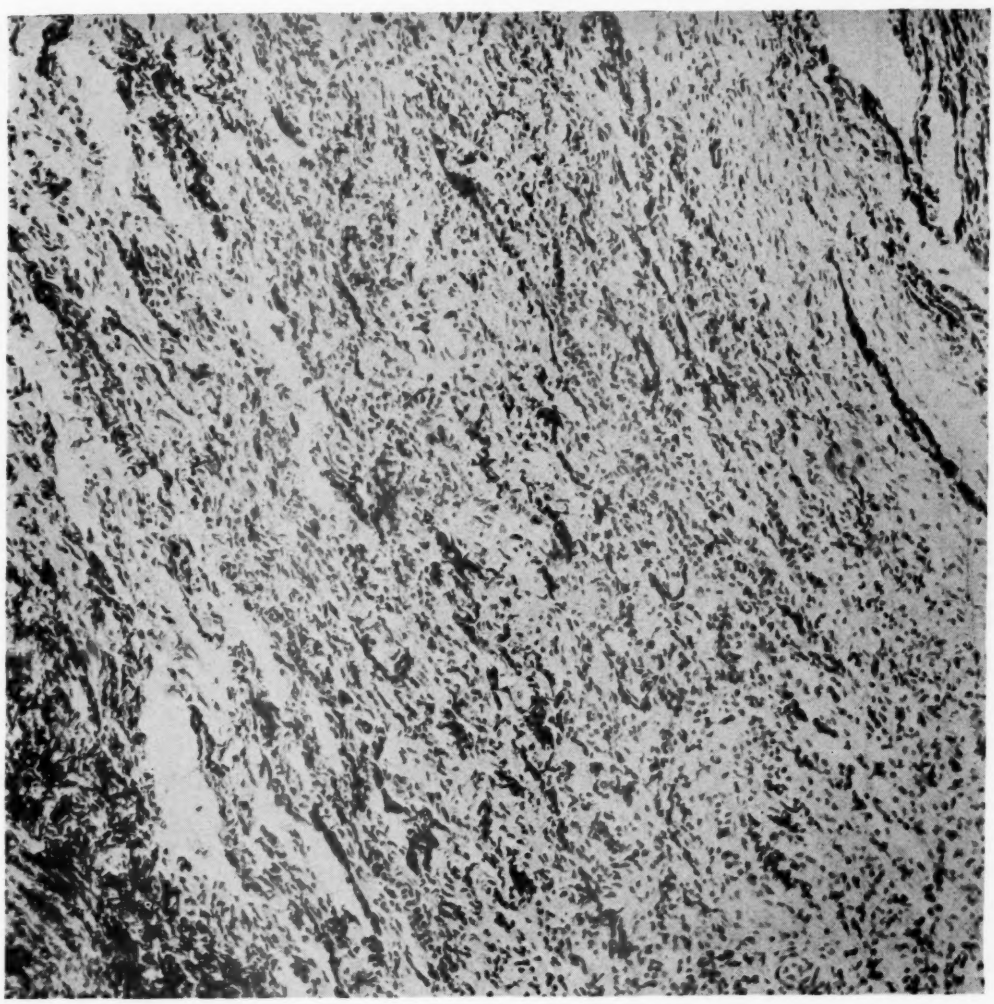


Fig. 4*A* (Case 6).—Neuroblastoma showing a four-year spontaneous remission, metastatic to liver (1943) and skull (1947). Photomicrograph of liver biopsy, atypical carcinoma.

We are increasingly conscious of the peculiar course of some malignancies and the difficulties in histologic diagnosis. The statement of a prognosis must always be a matter for extreme caution. A clinical lesson from our experience is illustrated by Case 6.

CASE 6 (132-163).—Neuroblastoma of undiagnosed origin, hepatomegaly and biopsy-proved liver malignancy, spontaneous four-year remission with terminal reactivation, metastases to skull and preauricular lymph nodes.

A 4-month-old male infant was admitted to the hospital in May, 1943, because of abdominal distention from the time of birth. The liver filled the right side of the abdominal cavity, with its lower border at the level of the iliac crest. Exploratory laparotomy revealed diffuse enlargement of the liver with an increase in its consistency. Liver biopsy was done and a histologic diagnosis was made of atypical carcinoma (Fig. 4, *A*). A poor prognosis was given and the infant was discharged from the hospital.

Fig. 4,*B* (Case 6).—Photomicrograph of frontal bone specimen, metastatic neuroblastoma.

Nine months later, he was seen again. There had been a 12 pound weight gain, and he was a normal appearing infant. The liver was palpable at the costal margin. Growth and development were normal for the next 4 years.

The second hospital admission was in 1947. An 8 by 5 by 6 cm. mass developed on the forehead (Fig. 4, *C*) following an injury one month before hospital admission. It was not fluctuant or pulsatile. There was radiologic evidence of involvement of the outer table of the skull. The liver was sharp-edged and palpable 1 cm. below the costal margin. A very vascular tumor which involved both tables of the skull as well as the dura was re-

moved. A histologic diagnosis of metastatic neuroblastoma was made (Fig. 4, *B*). One month later, a large preauricular lymph node was excised and the typical histologic picture of neuroblastoma was evident, in marked contrast to the atypical histologic characteristics of the liver biopsy done four years previously. The child died two weeks later.

In terms of a single pathologic process, the most likely sequence of events is as follows: a primary neuroblastoma of unknown origin with metastases to the liver, spontaneous clinical remission for more than four years with terminal widespread metastases to bone and soft tissues. The histologic diagnosis based on liver biopsy was indefinite, the prognosis based on liver biopsy was in error. In a similar instance, x-radiation therapy to the liver would seem to be advisable.[10]

PROPHYLACTIC TUMOR SURGERY IN CHILDREN

It is axiomatic, but nevertheless a statement of a fundamental concept in tumor surgery, that the undiagnosed mass should be treated as a malignancy until its exact nature is determined. It is interesting and valuable to know that a familial tendency has been observed in some cases. The notable examples of this are retinoblastoma, neurofibromatosis, and congenital polyposis of the colon. Case 7 illustrates this familial tendency.

Fig. 4,*C* (Case 6).—Photograph of the patient showing large tumor of the skull.

CASE 7 (3205).—Congenital polyposis of the colon with carcinomatous degeneration in multiple polyps, total colectomy with anastomosis of ileum to rectum, genealogy of four generations with fifteen deaths from the complications of polyposis.

A 54-year-old white man was admitted to the hospital in 1948 with symptoms of intestinal obstruction, bloody stools, and weight loss. A diagnosis of polyposis of the colon had been established by barium studies in 1931. The patient refused definitive treatment in 1942. Appendectomy was necessary in 1946 because of acute appendicitis and polyps were found in the surgical specimen removed at this procedure.

Barium studies on this admission confirmed the diagnosis of polyposis and showed an annular constricting lesion in the rectosigmoid. Multiple polyps were visualized at proctosigmoidoscopy. The metastatic survey was negative. In a three-stage procedure, total colectomy was done and the ileum was anastomosed to the rectum about 8 cm. above the anorectal line. Polyps below this level were treated by electrodesiccation. There were

three large ulcerating carcinomas in the surgical specimen, with carcinomatous change in innumerable adenomatous polyps that were examined. The patient is alive and well more than thirty months after the last surgical procedure.

The genealogy of the patient based on historical data is shown in Fig. 5. The detection of polyps of the colon and rectum depends on proctosigmoidoscopy and double-contrast barium enema radiographic studies. A very careful follow-up study of all members of this family is indicated.

A selected and important group of the so-called dangerous lesions of childhood will be discussed in the section to follow.

DANGEROUS LESIONS OF CHILDHOOD

Skin.—The clinical significance and close relationship between the so-called junctional nevus and melanoma has been stated by Allen[1] in a classical study. It is recognized that the junctional nevus develops, with adolescence, a high degree of malignant potential. The flat or elevated brown nevus of the skin which is situated below the level of the umbilicus, on the palmar surface of the hand, or the plantar aspect of the foot is a dangerous lesion at any age.

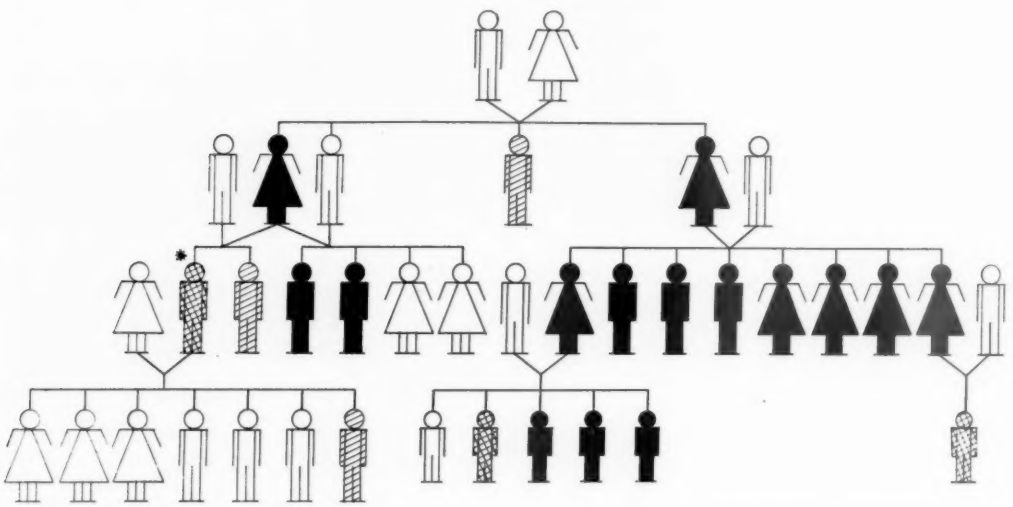
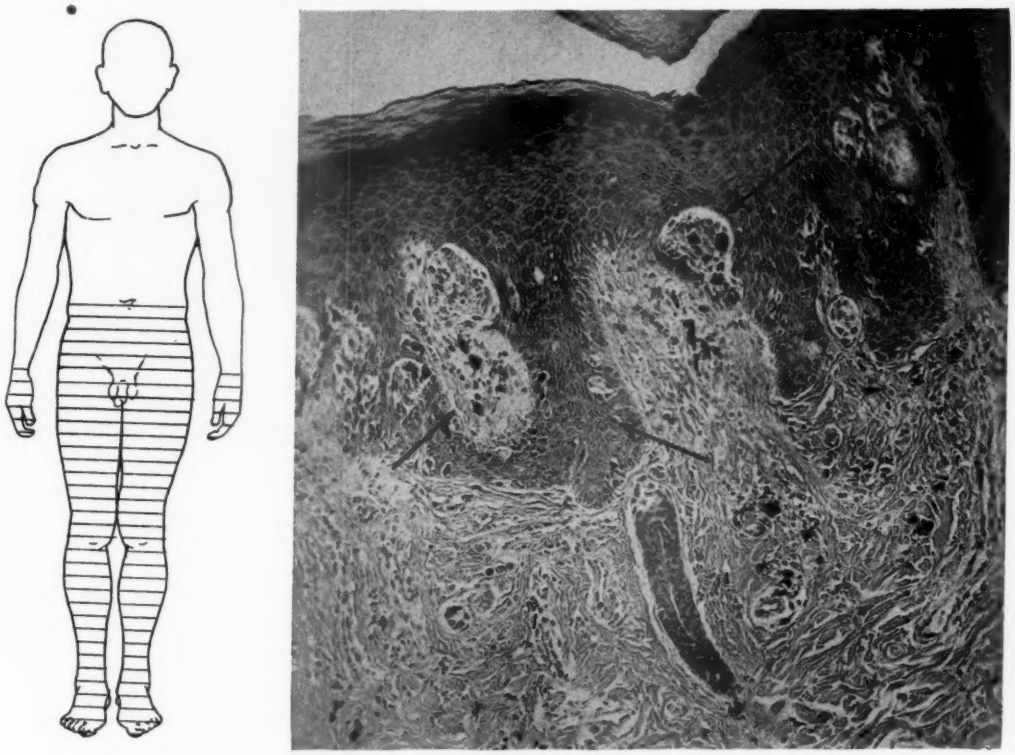


Fig. 5 (Case 7).—Genealogy of a patient* with multiple carcinomas superimposed on congenital polyposis of the colon.
Questionable cases (2), cross-hatched figures
Polyposis of colon (18), double cross-hatched figures plus black figures
Deaths from carcinoma (15), black figures

It should be excised before the age of puberty. A pigmented lesion in any location which demonstrates color change, accelerated growth, stinging, burning, or itching sensations may be undergoing malignant transformation. These findings are indications for a wide surgical removal of the lesion. Cavernous hemangioma and hemangioendothelioma show a tendency to infiltrate tissues and extend locally. The complications of ulceration and hemorrhage are not uncommon. The possibility of complete spontaneous regression of these vascular tumors is unlikely, in our experience, and their proper treatment is a problem for the surgeon, the radiologist, and the dermatologist.

Nerve Sheath Tumors.—The neurilemmoma (palisade-sheath tumors, perineural fibroblastoma, schwannoma) and neurofibromatosis (von Recklinghausen's disease) should be considered as premalignant tumors. The incidence of malignant change in these lesions is higher than generally realized.[11] In one series of forty patients with neurofibromatosis, nine died of neurogenic sarcoma, an incidence of malignancy of more than 22 per cent.[8] It would seem a worth-while precaution to remove all solitary nerve sheath tumors, those of more than 1.5 cm. in diameter, and lesions which show a tendency to enlarge with associated neurologic symptoms.



A. *B.*

Fig. 6.—*A.* Diagram of skin areas which show a high malignant potential for the development of melanoma from junctional nevi. *B.* Photomicrograph of junctional nevus undergoing malignant transformation.

Connective Tissue Tumors.—Lipoma, lipomatosis, fibroma, lipofibroma, chondroma, and osteochondroma are benign tumors which may undergo a transition to sarcoma. It is well to guard against this possibility by removing solitary chondromas and other connective tissue neoplasms, particularly if the tumor is bulky, gives rise to subjective symptoms, or if it is subject to trauma.

Embryonal Tumors.—The dermoid cyst and teratoma assume an important place in any discussion of premalignant lesions of childhood. The more complex the structure of the tumor, the more likely the possibility of malignancy. A diagnosis of benignancy is always made with considerable reservation, even after the most careful histologic study of the tumor. The complex teratoma

should be considered as a tumor which possesses a high malignant potential or is actually malignant. Proper treatment is by surgical excision. The prognosis depends upon the patient's survival of the operation and should be made with caution.

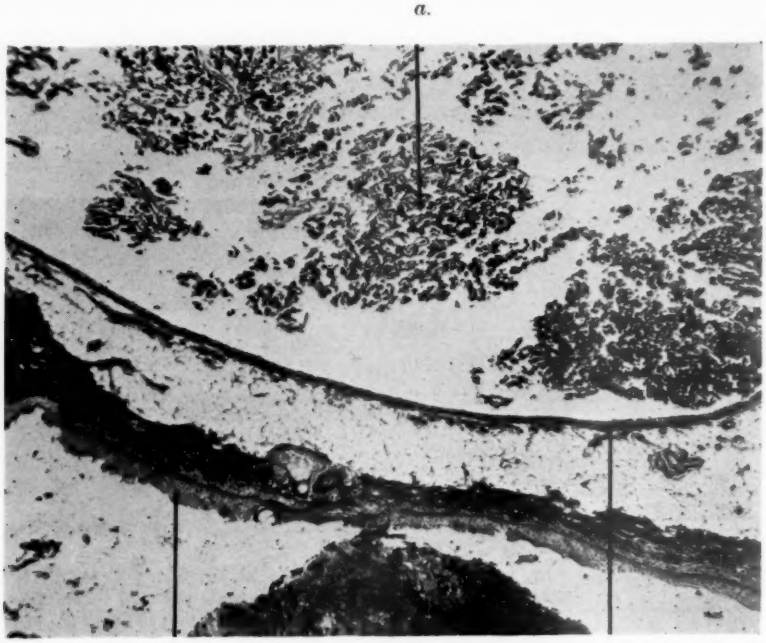


Fig. 7,*A* (Case 8).—Photomicrograph of ovarian teratoma, histologically benign; *a*, ependyma-like tissue, *b*, squamous epithelium, *c*, ciliated epithelium.

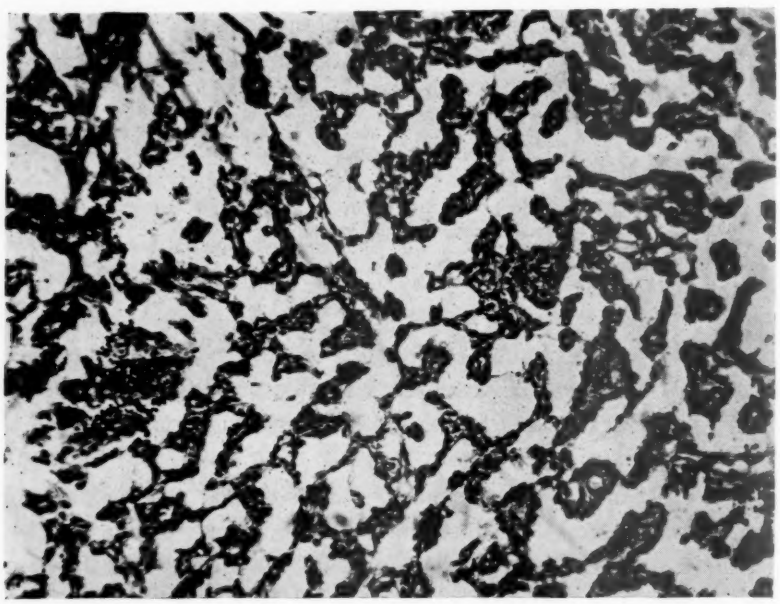


Fig. 7,*B* (Case 8).—Photomicrograph of omental biopsy showing metastatic papillary carcinoma from the ovarian teratoma (higher magnification).

Fig. 8 (Case 9).—Anteroposterior and lateral roentgenograms showing the characteristic posterior-superior mediastinal location for a ganglioneuroma. Asymptomatic tumor diagnosed at mass survey chest x-ray examination.

CASE 8 (G4614-49).—Complex ovarian teratoma complicated by hemorrhage into the tumor; exploratory laparotomy and oophorectomy, death in three weeks from fulminating carcinomatosis peritonei.

A 9-year-old girl was well until September, 1949, when she developed acute abdominal pain and a palpable abdominal mass following trauma to the abdomen. A 15 by 12 by 7 cm. hemorrhagic, cystic-solid tumor of the right ovary was removed at exploratory laparotomy. There was no evidence of metastatic spread from the lesion. The histologic diagnosis was teratoma of the ovary with focal necrosis and inflammation (Fig. 7, *A*). The microscopic appearance of malignancy was not evident, but it was stated by the pathologist that a guarded prognosis should be given.

Several days later, a second operation was done because of massive intraperitoneal hemorrhage. The cause for this was evident at laparotomy. A friable, vascular, metastatic tumor completely filled the peritoneal cavity. A histologic diagnosis of metastatic papillary carcinoma from a teratoma of the ovary was based on omental biopsy (Fig. 7, *B*).

Masses of the Head and Neck.—The early diganosis of retinoblastoma can be made in about one-half of the cases by routine postnatal ophthalmoscopic examination, according to Gaisford.[7] The solitary adenoma of the thyroid gland is more likely to be malignant in the child than in the adult, and its discovery is an indication for its removal. Branchiogenic cysts and sinuses and teratomatous masses in the neck should be excised.

Mediastinal Tumors.—The problem of the asymptomatic mediastinal tumor assumes increasing importance with the introduction of mass survey chest x-ray examinations. The most common tumors encountered are the neurofibroma, ganglioneuroma, dermoid cyst, and teratoma. The mediastinum should be considered as a critical anatomic area. The specific tumor that will degenerate, perforate, or cause extensive destruction of vital structures by pressure and local invasion cannot be predicted. Moreover, it is estimated that at least 10 per cent of benign mediastinal tumors will undergo malignant transformation.[20] Exploratory thoracotomy and surgical removal are indicated.

CASE 9 (175-146).—Asymptomatic posterior-superior mediastinal tumor revealed by survey chest x-ray examination, thoractomy, and removal of ganglioneuroma.

A 14-year-old boy was admitted to the hospital for exploratory operation because of a mediastinal tumor that had been discovered by routine chest survey x-ray examination (Fig. 8). He was asymptomatic. There were no cafe-au-lait spots on the skin, peripheral nerve tumors, or other stigmas of neurofibromatosis.

A well-circumscribed, 11.5 by 7.5 by 7 cm. solid tumor was removed from the posterior-superior mediastinum without incident. The postoperative course was uncomplicated. A histologic diagnosis of ganglioneuroma was made.

Tumors of the Abdomen.—In the very young, neuroblastoma and Wilms' tumor are most frequent. Exploratory laparotomy should follow the discovery of an abdominal mass with a minimum of delay. Traumatic manipulative procedures in the preoperative period are to be discouraged and extensive investigative studies are usually not indicated. It is not our policy to recommend preoperative x-radiation for neuroblastoma or Wilms's tumor.

Adenomatous Polyps.—Helwig[9] has discussed the evolution of adenomas of the large intestine and their relation to carcinoma. Swinton and Warren[21] were able to demonstrate a histologic transition from normal mucosa to adenocarcinoma in 14 per cent of all their cases of carcinoma of the colon and rec-

tum, and they estimated that a much higher percentage of malignant change in the colon and rectum than this arises in previously benign polypoid tumors. The premalignant nature of adenomatous polyps is especially striking in the case of congenital polyposis of the colon.[12]

Ectopic Testis.—The chance of malignant change developing in the undescended testicle is increased approximately fifty times over this chance in the normally situated testis.[14] The inguinal or abdominally placed testicle is a real cancer hazard in the adult. The ectopic testis should be removed if it cannot be placed in the scrotal sac by appropriate surgical techniques.

Penile Carcinoma.—Wolbarst[22] has stated that circumcision of every male child in infancy would virtually eliminate the possibility of penile carcinoma.

SUMMARY AND CONCLUSIONS

1. The high mortality of proved malignancies of childhood and the demonstration in recent years that the operative risk of major surgical procedures is not excessive suggest that a more radical surgical approach to the problem of the malignancies of childhood is warranted.

2. On the basis of our experience with unexpected long-time survivals of children having apparently inoperable or incompletely removed malignant tumors, as well as the biologic unpredictability of pediatric tumors based on histologic study, we have been led to revise our concepts of x-radiation therapy in this age group. A liberalization of the indications for cancerocidal x-radiation seems justified. The general indications for x-radiation therapy in our clinic are tabulated.

3. Criteria of malignancy and pitfalls in the histologic diagnosis of pediatric tumors have been discussed. A clinicopathologic classification of the tumors of childhood is presented.

4. The clinically malignant nature of some benign tumors and the possibility of malignant change in others indicate the advisability of prophylactic removal of the so-called "dangerous lesions of childhood."

5. A survey has been made of 175 tumor case admissions to the Doernbecher Memorial Hospital for Children during a three-year period from 1946 to 1949. A series of illustrative case histories is reported.

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COMBINED ABDOMINOPERINEAL EXCISION OF THE RECTUM—A PLAN FOR STANDARDIZATION OF THE PROXIMAL EXTENT OF DISSECTION

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THERE appears to be no unanimity among writers as to the extent of proximal dissection in the combined abdominoperineal excision for carcinoma of the rectum. In his Lettsomian lecture, Miles[1] described the elective site of ligation of the inferior mesenteric artery to be at a point between the areas of distribution of the first and second sigmoidal branches of the inferior mesenteric artery. The reason this site was chosen has never been made clear, but it is probably related to the question of impaired circulation at Sudek's critical point.[2] The importance of this point, however, in combined abdominoperineal resection where the greater part of the sigmoid colon is sacrificed, is of no moment. Furthermore, for a number of reasons, such as anatomic variations in the origin of the sigmoidal branches and heavy deposits of fat between the leaves of the mesacolon, it is difficult to ascertain this elective site and the surgeon usually proceeds to ligate the superior hemorrhoidal vessels at the level of the promontory of the sacrum or bifurcation of the aorta.

The careful studies of the pathways of lymphatic spread in carcinoma of the rectum by Gilchrist and David[3] and Coller, Kay, and MacIntyre[4] also point to the invalidity of limiting the extent of proximal resection to the elective site of ligation as suggested by Miles. Since 1945[5] I have extended and standardized the proximal extent of dissection in the combined abdominoperineal resection for carcinoma of the rectum and the purpose of this publication is to describe the surgical technique devised.

SURGICAL TECHNIQUE

Preoperative Preparation.—Careful attention is paid to the patient's general physical status, state of nutrition, hydration, electrolytic balance, hemoglobin value, bleeding, and clotting times. Sufficient time is taken in the preparation of the patient to place him in the best possible physical condition for operation. In the earlier cases no intestinal antibiotics were used, but recently we have utilized aureomycin in doses of 1 Gm. every twenty-four hours for three days prior to operation. The bowel is also cleaned carefully and completely by means of repeated tap water enemas the night before and the morning of operation. The patient's lower extremities are wrapped with rubber elastic bandages, a nasal tube is inserted and a catheter is placed in the urinary bladder. Before

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the patient is anesthetized an intravenous drip is started through a needle inserted into one of the veins of the upper extremity.

Anesthesia.—Pentothal-curare mixtures given intravenously, with oxygen administered through an intratracheal tube, have been used in all cases.

Operative Technique.—A left "hockey stick" incision (Fig. 1) is used with a vertical paramedian component beginning at the symphysis pubis and extending to just below the umbilicus. The oblique portion of the incision extends from this point to the costal margin at about the level of the anterior tip of the

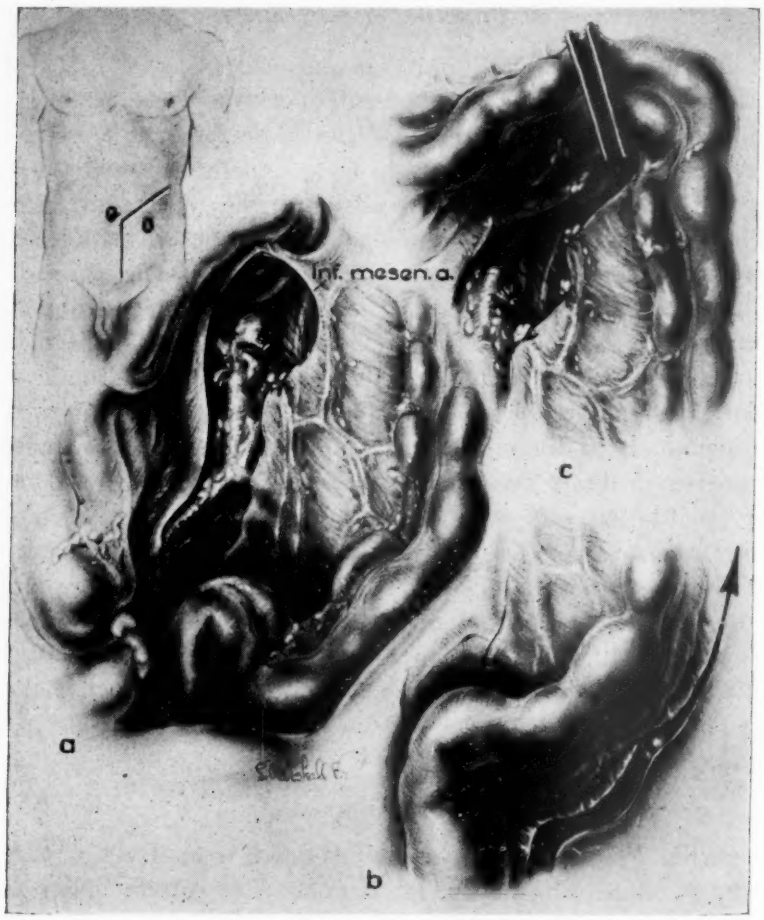

Fig. 1.—Insert shows "hockey-stick" incision. Site of the colostomy is either at the umbilicus or lateral edge of the left rectus muscle. *a,* Ligation of inferior mesenteric artery at origin of aorta and incision of posterior peritoneum from level of duodenum to pelvic mesacolon. *b,* Mobilization of lateral leaf of parietal peritoneum in region of sigmoid colon. *c,* Transection of transverse colon and incision of transverse mesacolon.

ninth rib. In the lower portion of the incision, the anterior rectus sheath is incised and the rectus muscle is retracted intact, laterally. In the oblique portion of the incision the rectus muscles and the lateral abdominal wall muscles and their respective fascias are incised in the direction of the incision. This incision gives a wide exposure of the field and particularly permits the dissection of the splenic flexure under direct vision.

After the abdomen is opened, careful examination is carried out to determine the operability of the lesion and the presence or absence of regional lymph node metastasis and/or liver metastasis. In the main, a very aggressive attitude toward removal of the lesion has been adopted, even though it is obvious that a palliative type of resection is being done. The primary dissection is carried out to isolate the inferior mesentery artery as it arises from the aorta. This vessel is transected between forceps and doubly ligated using stick ties of 30 silk (Fig. 1, *a*). The posterior parietal peritoneum is incised to the right of the aorta over the inferior vena cava from the level of the third portion of the duodenum down into the true pelvis where the pelvic mesacolon arises. The latter is incised laterally at the pelvic brim so that the entire mesacolon is removed. The parietal peritoneum to the left of the pelvic and descending colon is incised and the dissection is continued to mobilize the splenic flexure and lateral one-quarter of the transverse colon (Fig. 1, *b*). The latter is then transected and the transverse mesacolon is incised obliquely and inferiorly to meet the initial incision of the peritoneum at the level of the third portion of the duodenum (Fig. 1, *c*). The lateral one-quarter of the transverse colon, the descending colon, and the pelvic colon with their respective mesenteries and contained lymph nodes are dissected inferiorly (Fig. 2, *a* and *b*). Care is taken to identify both ureters throughout the entire extent so as to avoid injury to them. The lymph nodes of the anterior and lateral aspects of the aorta and inferior vena cava, from the level of the third portion of the duodenum down to the bifurcation of the aorta into the common iliac arteries, are then dissected. This dissection is carried out in a readily entered plane between the adventitia of the aorta and the surrounding periadventitial tissues containing in addition to lymph nodes the pre-aorta sympathetic nerve plexuses and loose connective tissues. This plane is relatively avascular, with only occasional small nutrient vessels to the lymph nodes being encountered in the dissection. The bleeding which arises from this source is best controlled by means of pressure with a gauze sponge and at no time is it particularly profuse or troublesome. Care is taken to dissect out the lymph nodes along both common iliac arteries—this necessitates mobilization of vessels so that the lymph nodes that are placed posteriorly may also be removed as well as those lymph nodes more readily available along the anterior, superior, and inferior aspects of these arteries. The lymph nodes along the sacrum below the bifurcation of the aorta are taken as the dissection continues into the pelvis. The mobilization of the rectum, the dissection lateralward, including the levator ani, and the dissection in the perineum inferiorly are done in the standard fashion as advocated by Miles.[1] Hemostasis is checked carefully and the reconstitution of the pelvic floor by mobilization of the residual portion of the peritoneum of the lateral wall of the false pelvis is begun and carried out utilizing interrupted 30 silk for approximation (Fig. 2, *a*). Because of the extent of removal of peritoneum of the posterior abdominal wall, it is not possible to approximate the peritoneal edges at this level. No effort is made to do so. The transverse colon is brought out as a colostomy either through

the umbilicus, after excising it, or through a separate stab wound in the left lower quadrant at the lateral edge of the rectus sheath (Fig. 1 insert). The peritoneum and anterior and posterior rectus sheath are sutured carefully to the circumference of the bowel, using interrupted 40 silk, with care being taken to place the sutures in a serosa or appendices epiploicae, not through the bowel wall. The abdominal incision is closed in layers using interrupted 30 silk.

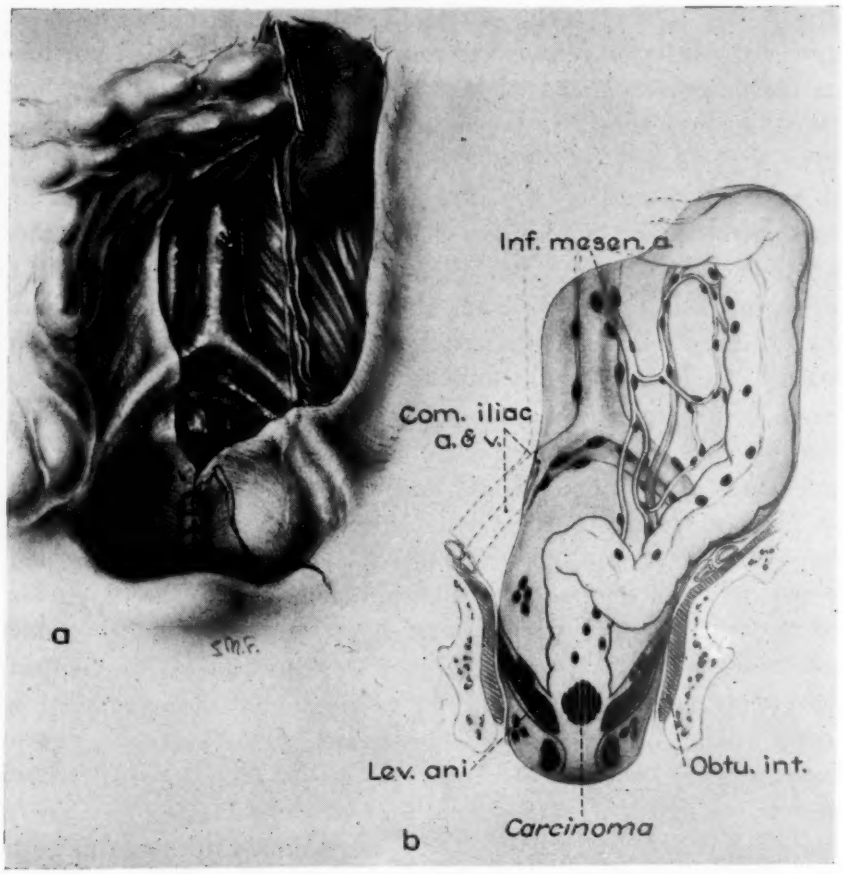

Fig. 2.—*a*, Removal of lateral one-fourth of transverse colon, descending colon, and sigmoid colon with respective mesacolons. Clean dissection of lymph nodes from anterior and lateral aspects of aorta and inferior vena cava from level of duodenum to bifurcation. Removal of lymph nodes from around the common iliac arteries. Beginning reconstitution of pelvic floor with interrupted silk sutures. *b*, Schematic diagram indicating the extent of lymph node dissection and removal of colon and mesacolon distal to lateral one-fourth of transverse colon.

Postoperatively the daily fluid and electrolytic requirements are met and blood transfusions are given if indicated. Parenteral administration of antibiotics is usually carried out for the first four days and the nasal tube is also left in for this length of time. The clamp on the colostomy is permitted to slough off; this usually occurs on the third or fourth day and only if there is marked distention is a catheter placed in the colostomy prior to this time. The average length of the stay in the hospital has been twelve days.

DISCUSSION

There is ample evidence to show that the migration of cancer cells into the extramural lymphatics is frequent in cancer of the rectum even when the lesion is small. Where careful studies have been carried out on cleared specimens it has been shown that: (1) The absence of palpable lymph nodes does not rule out metastasis to lymph nodes. (2) The sequence of involvement of lymph nodes is not an orderly progression from proximal to distal lymph nodes. There may be large skip areas, that is, lymph nodes in juxtaposition to the tumor may be involved and no others found except those about the inferior mesenteric arterial stem.[3, 4] Our studies, as well as those by Rosi,[6] indicate that lymph nodes in the mesentery of the descending colon may be involved even though the primary neoplasm is in the rectum. The majority of the efferent lymphatics in the rectum pass upward and consequently the most constant and, therefore, the most important of all modes of spread is in the proximal direction.[3] Further support for this thesis of the desirability of more extensive proximal dissection in the combined abdominoperineal resection comes from the observations of Wangensteen and Lewis,[7] who are practicing "second look" operations upon patients with carcinoma of the rectum who have had lymph node metastasis at the first operation. In approximately 60 per cent of these patients focal metastases, that might have been removed if a more extensive proximal resection had been done initially, have been found along the aorta on the second or third operation.

In view of the previously mentioned facts, it seems reasonable to suggest that the extent of proximal resection should be extended in the manner described for all carcinomas of the rectum, not merely for those with palpable lymph nodes. The removal of the lymph nodes along the stem of the inferior mesentery artery as well as along the aorta and inferior vena cava from the duodenum downward, and also the removal of the mesenteries of the descending and pelvic colons, appears to be in order. The additional dissection needed is not difficult and does not prolong the operation unduly. The colostomy, fashioned from the transverse colon, behaves no differently than one made from the sigmoid colon from the standpoint of solidity of stool or its daily control. Since many advantages and no apparent disadvantages appear at this operation, it seems reasonable that it should be accepted as a standard procedure for all carcinomas of the rectum.

SUMMARY

A technique for standardizing and extending the proximal dissection in the combined abdominoperineal operation for carcinoma of the rectum is presented. The lateral one-fourth of the transverse colon, descending colon, and pelvic colon is removed along with the respective mesenteries, as well as the lymph nodes along the anterior and lateral aspects of the aorta and inferior vena cava from the level of the third portion of the duodenum distalward. Careful dissection about the common iliac arteries is carried out to remove the lymph nodes that may be found posteriorly as well as anteriorly, superiorly, and inferiorly along these vessels. The patient is left with a transverse colostomy, but the

solidity of the stool and its daily control differs very little, if at all, from a sigmoid colostomy. The operation meets the dictates of a good cancer operation for cancer of the rectum far better than the standard Miles combined abdominoperineal resection, for it is based on the anatomic distribution of lymph nodes that drain the efferent extramural lymphatics of the rectum as well as on the known pathways of proximal metastatic spread of carcinoma of the rectum.

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FASCIA LATA TRANSPLANTS FOR RESECTED CERVICAL ESOPHAGUS

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THE diversity of procedures that has been suggested for the treatment of carcinoma of the cervical esophagus and the hypopharynx attests to the difficulty of its cure and the ingenuity of the modern surgeon. Of most recent interest are procedures in which the stomach is transposed to the chest and neck,[1] the use of a neck skin flap,[2-4] the use of tubed pedicle grafts,[5] and the use of intestinal segments to bridge large gaps.[6] The ideal method of reconstruction of the esophagus would seem to be end-to-end anastomosis as performed in benign lesions and in tracheo-esophageal fistulas. However, whether this procedure would lend itself to large defects of the esophagus and to the general philosophy of cancer surgery still remains to be seen. Suffice it to say that, in general, the recurrence rate in true cervical esophageal carcinoma and in hypopharyngeal carcinoma (retrocricoid) is great, not only because of spread to the cervical lymph nodes, but also because of direct spread into the near-by sheaths of the neck. Rational cancer surgery in this area would necessitate the removal of the lesion and bilateral neck dissection.

The substitution of metallic and Polythene tubes for large defects of the trachea in the experimental animal has been tried recently by Clagett and associates[7] and Daniel.[8] Hohmeier[9] and Neuhof[10] have closed small windows in the trachea with the use of free fascia lata. We should like to present a studied case in which a tube of tantalum gauze covered on both sides by fascia lata was inserted into the neck to close a gap of 8 cm. left following resection of the cervical esophagus and pharynx. This method was first performed on a human being by Rob and Bateman.[11] Evidence of complete epithelization in the following case was obtained by pathologic studies.

CASE REPORT

Mrs. E. R. L. (A. H. No. 167272), a 68-year-old white woman, was referred to the Ancker Hospital on March 15, 1950. This woman was perfectly well until January, 1950, at which time she noted a peculiar noise upon swallowing. About 1 month previous to admission she began to notice difficulty in swallowing solid foods, but had no trouble with liquids. She had lost about 5 pounds, but had not felt weak, nor had she any pain. Five years previous to this admission, a thyroidectomy had been performed.

Physical examination was essentially negative. The cardiorespiratory and renal statuses were good. Esophagoscopy and biopsy revealed a squamous-cell carcinoma of the cervical esophagus involving the posterior area of the cricoid cartilage and extending for 2 cm. down the esophagus.

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Operative Procedure (March 21, 1950).—By means of a transverse collar incision, the trachea and esophagus were exposed. It was soon seen that the larynx was involved; therefore, the larynx up to the epiglottis, the cervical esophagus and lower pharyngeal esophagus, and a good segment of trachea were removed. This was done in such a manner that we were well around the gross lesion. This left a defect of about 8 cm. in the esophagus (Fig. 1).

The right thigh had been previously draped, and a segment of fascia lata was removed. This was then sewn about a cylinder of tantalum mesh in such a manner that the mesh was completely covered on the outside and the ends. The only portion of the mesh that was left uncovered was within the cylinder. The cylinder was so sutured that the esophageal mucosa extended for a distance of 0.5 cm. down the outside of the cylinder. About 8 silk sutures were used at each end.

A permanent tracheostomy through a separate incision was then made and the wound closed. Three Penrose drains were left in place. A plastic nasal tube was placed through the anastomotic area into the stomach for feeding purposes.

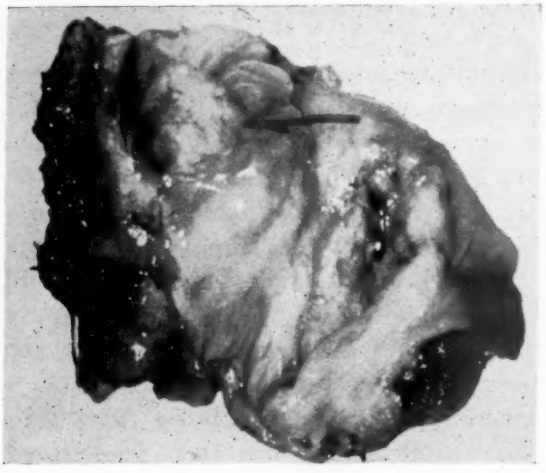
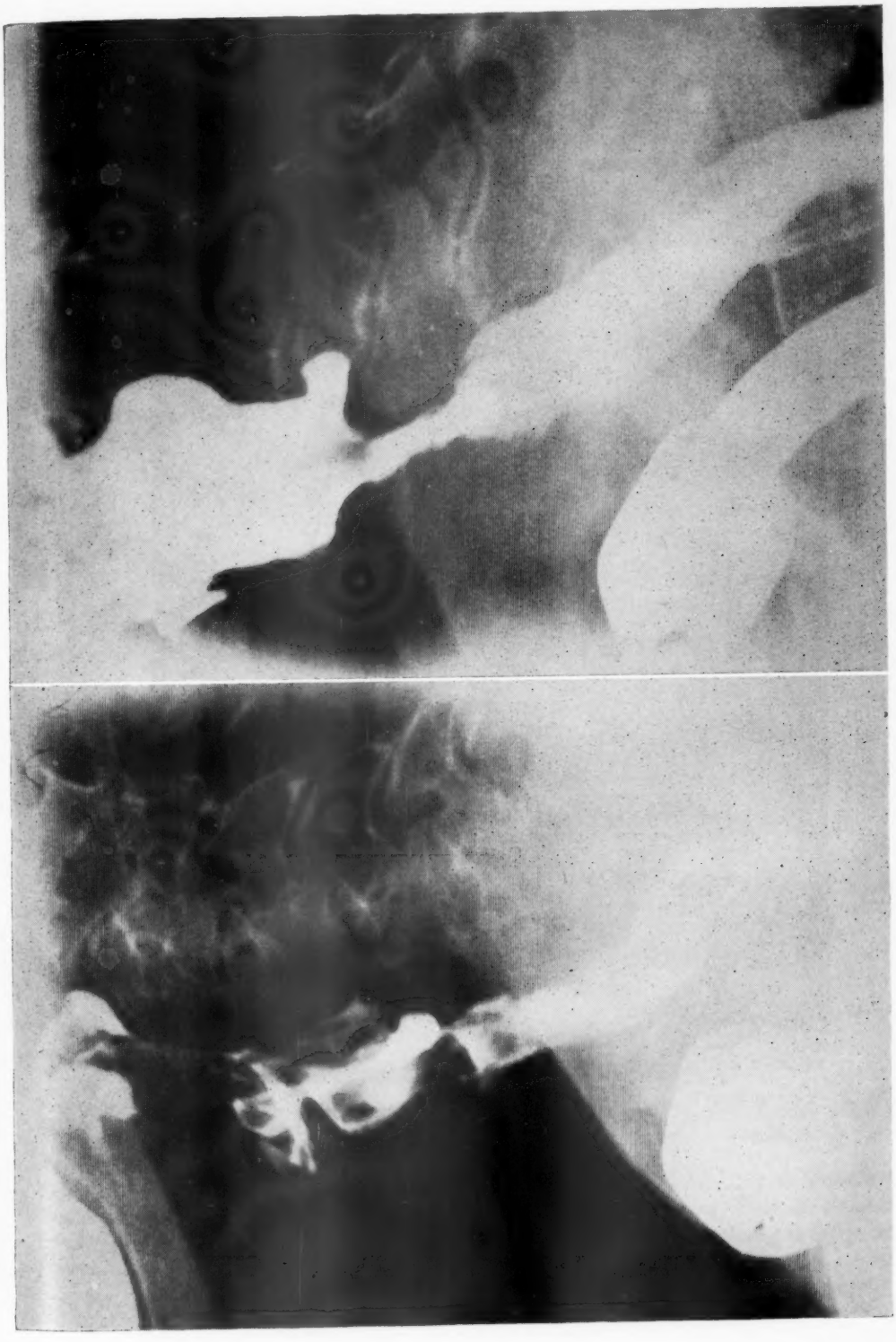


Fig. 1.—Resected specimen of cervical esophagus and larynx.

Postoperative Course.—A high-protein mixture, fed via the nasal tube, was tolerated very well. Mucous plugs, which at times were serious, formed in the trachea. This was relieved by steam inhalations. Periodic chest plates were taken during the convalescence which was excellent. On April 24, 1950, a roentgenogram revealed that the tantalum mesh which had been easily noticed previously was now missing. A film of the abdomen failed to reveal its presence. We were perplexed at the disappearance of the mesh. Further checking of the nurses' notes revealed that it had apparently been passed on April 19, 1950, and had been recorded as a "hard, triangular stool about 3 inches in length." Up to that time the stools were soft.

The nasal feeding tube was removed on May 1, 1950, and she was able to swallow liquids well. She was gradually put on a regular diet. However, it was apparent that dilatations would be necessary periodically until graft was completely epithelized.

A barium swallow roentgenogram (Fig. 2) on May 12, 1950, revealed that the barium passed freely throughout the entire esophagus with no evidence of any obstruction. An area of minimal narrowing was noted approximately 5 cm. distal to the upper anastomosis, in all likelihood representing a small constriction at the area of anastomosis following surgery. This area appeared to dilate with the passage of barium, and no definite evidence of any delay in passage at this area was evident either at fluoroscopy or on the subsequent films. Esophagoscopy was performed intermittently, and it was noted that the graft was being covered with epithelium both from above and below.



A. *B.*

Fig. 2.—*A*, Barium swallow roentgenogram of area replaced by fascia lata showing motility through the segment. *B*, Barium swallow roentgenogram after barium had passed the resected area.

Following her discharge on May 21, 1950, the patient was readmitted on June 4, 1950, for a right radical neck dissection. In the interval she had been dilated twice weekly and was able to eat quite satisfactorily. Following the neck dissection, she was discharged on June 16, 1950. She was then seen periodically in the outpatient clinic and dilated. A 46 French dilator was passed with difficulty, but smaller ones, 40 and 36 French, were passed much more easily. She was able to eat normally and felt well.

On July 27, 1950, in the outpatient clinic, a chest plate showed the presence of multiple lung nodules which were very suggestive of metastasis, yet the only complaint was some dyspnea. Further roentgenograms during the ensuing weeks revealed further extension of these nodules, though clinically she was not failing fast. She died suddenly on Sept. 8, 1950, while carrying a large basket up a flight of stairs.

Fig. 3.

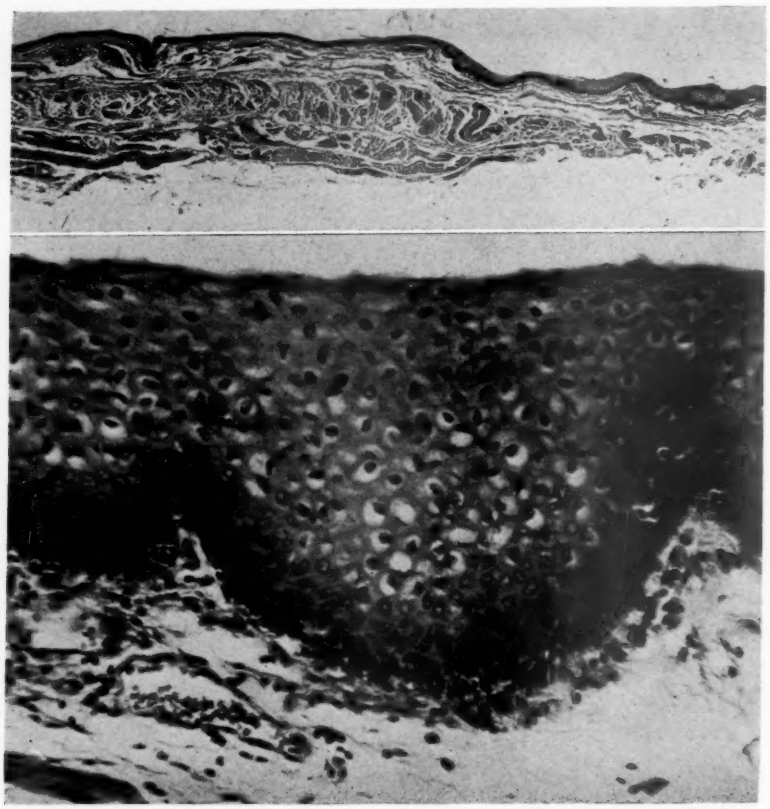


Fig. 4.

Fig. 3.—Low-power magnification of longitudinal section of transplanted segment showing complete epithelization.

Fig. 4.—High-power magnification of mucosa overgrowing fascial transplant.

We were very fortunate in being able to obtain post-mortem specimens.* Extensive metastases to the liver and lungs were present. Of significance were the following findings† regarding the fascia lata transplant: The fascia lata transplant was completely epithelized with normal squamous epithelium. Grossly and microscopically this could not be distinguished from normal esophageal mucosa except for the absence of submucosal glands which are normally present (Figs. 3, 4, and 5).

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†By Dr. John F. Noble.

DISCUSSION

The rebuilding of exenterated portions of the intestinal tract is a problem which probably will be solved in the near future. The case presented illustrates this possibility.

It was interesting to note that fistulous communication did not occur. Even if it did occur, appropriate treatment would probably have closed it off. The fact that epithelization was occurring and eventually would have grown over an area of breakdown in the graft seems to bear this contention out. The presence of the tantalum mesh acts only as a cylindrical support for the fascial

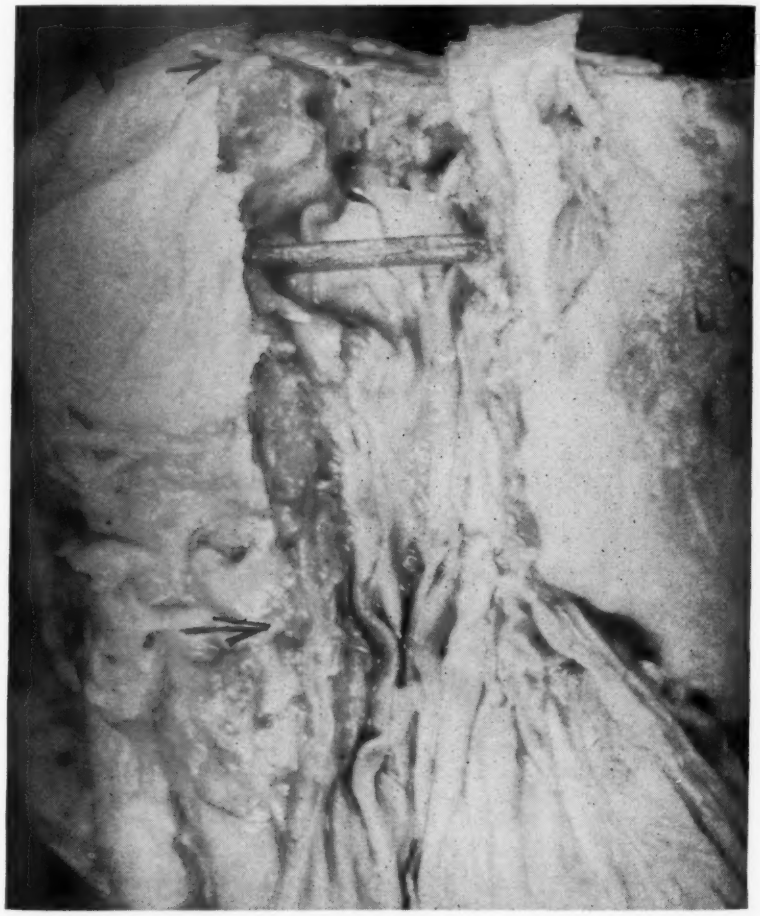

Fig. 5.—Gross specimen showing the esophagus opened longitudinally and the area replaced by fascia (between 2 arrows) covered with normal epithelium.

graft until the tissues in the surrounding area are able to take over this function. The epithelium then grows onto the fascial surface which does not disintegrate. Experiences with fascia lata grafts in the treatment of large hernia defects led us to believe this to be true. Biopsies of these grafts months afterward revealed normal fascia. The normal nutrition of fascia lata requires few or no immediate adjacent blood vessels; lymphatic and intercellular juices are sufficient.

The passage of the tantalum mesh by rectum was indeed a surprise to us. Had it not occurred, we were prepared to remove it by esophagoscopy. The presence of mesh rather than a solid frame would not have made this a difficult problem, as there would have been only tiny multiple points of attachment rather than a large fixed surface.

This experience seems to suggest that this method might also be used for large tracheal defects as was done by Rob and Bateman. It also suggests that it may be used in those cases of tracheo-esophageal fistula in which there is too great a gap between the proximal and distal esophageal ends for primary anastomosis.

SUMMARY AND CONCLUSIONS

1. A case of cervical esophageal carcinoma is presented, in which resection of the esophagus and larynx was performed.

2. A tube of tantalum mesh covered on the outside by fascia lata was inserted in the esophageal gap. The gap extended for a distance of 8 cm. The tantalum mesh was extruded per rectum about 1 month later.

3. Gross and microscopic evidence of complete epithelization of this graft was obtained about 6 months later upon death of the patient from extensive visceral metastases.

4. During her life the patient needed periodic dilatations but was able to partake of normal foods.

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THE EFFECTS OF VARIOUS HYPERTONIC SODIUM SALT SOLUTIONS ON CISTERNAL PRESSURE

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VARIOUS hypertonic solutions are used to lower intracranial pressure; their usefulness is limited somewhat. For example, hypertonic glucose solutions produce a secondary rise in intracranial pressure after the initial fall.[1] Hypertonic sucrose solutions lower the pressure and do not induce a secondary rise; however, the repeated use of large amounts may cause severe renal tubular injury.[2] Hypertonic solutions of magnesium salts are capable of inducing fairly well-sustained drops of intracranial pressure, but they are concomitantly capable of profound depression of the central nervous system. Various hypertonic sodium salts* were used experimentally by Weed and McKibben,[3] but when they are given in the concentrations suggested by their experiments, respiratory and cardiovascular disturbances tend to occur.

These studies were conducted in an attempt to find a solution of low toxicity which is capable of effectively lowering intracranial pressure without producing a secondary rise.

METHODS

Fifteen mongrel dogs were used and several experiments were performed on each animal. The dogs were anesthetized initially with sodium pentobarbital; subsequently light anesthesia was maintained by intraperitoneal injections of the same drug.

With the dog in a horizontal position lying on its right side, the intracisternal pressure was measured by means of a malleable No. 18 spinal needle introduced through the atlanto-occipital ligament into the cisterna magna and connected to a vertical manometer of 1 mm. bore. The manometric system was filled with 0.9 per cent saline solution and the needle was connected to the manometer by means of a fine glass adapter. This maneuver was usually performed with the loss of about 2 drops of cerebrospinal fluid. Twenty or 30 minutes were allowed to elapse for stabilization of the cisternal pressure. The mean femoral arterial blood pressure was measured with a mercury manometer. All intravenous infusions were given through a cannula in the left femoral vein. Blood samples were drawn from the right femoral vein. An 18 French catheter was placed in the bladder; the rate of urine flow, the specific gravity of the urine, and the rectal temperatures were recorded every 15 minutes.

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*NaCl, Na_2SO_4, $NaHCO_3$.

The sodium concentrations in serum and urine were determined by the Beckman flame photometer and by the gravimetric method of Butler and Tuthill.[4]

The iso-osmotic* solutions used in this study were molar sodium chloride (5.8 per cent), molar sodium lactate (11.2 per cent) and two-thirds molar sodium succinate (18 per cent). Two molar glucose (36 per cent) was used in one experiment and 1.39 molar (25 per cent) glucose in others.

The animals were first anesthetized and the apparatus arranged as described. The intracisternal pressure was then increased by the infusion of a 5 per cent dextrose solution (7 ml. per kilogram body weight). Following the cessation of the subsequent diuresis and the stabilization of the cisternal pressure, one of the hypertonic sodium salt solutions was given at a rate of 10 ml. per minute. The total amount given as a unit dose amounted to 7 ml. per kilogram of body weight. Usually more than one solution was tested on each dog; during the interval between the injections of the hypertonic solutions, infusions of 5 per cent dextrose were given to effect the return of the intracranial pressure to the level obtaining before the preceding injection of the hypertonic fluid. Samples of blood were taken just before the injection of any solution.

RESULTS

The mean intracisternal pressure in the normal anesthetized dogs was found to be 100 mm. of saline solution. After the initial infusion of 7 ml. of 5 per cent glucose in water per kilogram of body weight the mean intracranial pressure rose to 194 mm. of saline. Forty-five to 60 minutes were required for the completion of the primary pressure change. The cisternal pressure began to fall during the infusion of the hypertonic sodium salt solutions; the maximum decrease of intracranial pressure was obtained in about 30 minutes. During the injection of hypertonic glucose solutions the intracisternal pressure underwent a short-lived fall; this fall was immediately followed by a rise that ultimately attained a level far above the control pressure. The relative effectiveness of the hypertonic solutions subjected to investigation is shown in Table I.

TABLE I

SOLUTION	MOLAR	CHANGE IN CISTERNAL PRESSURE (MEAN MAXIMAL) (MM. SALINE)
Sodium succinate	⅔	-96
Sodium lactate	1	-99
Sodium chloride	1	-95
Glucose	2	+69

In a series of experiments that were conducted without the primary injection of 5 per cent glucose in distilled water the decreases in intracisternal pressure were practically of the same magnitude as those shown in Table I.

*Checked by freezing point determinations.

Following the infusion of the hypertonic salt solutions, the cisternal pressure remained depressed for 2½ to 4 hours; the pressures then became stabilized at or below those levels attained before the injections. In 2 instances the pressure returned to a point that was slightly above the control level.

The blood pressure did not change when 5 per cent glucose in water was administered between the injections of the hypertonic salt solutions. In a few instances, the rectal temperatures rose from 3 to 5 degrees Fahrenheit following the injection of the hypertonic salt solutions under these conditions.

When the hypertonic salt solutions were injected at hourly intervals and 5 per cent glucose in water was not given the blood pressure fell progressively and ultimately attained shock levels; the rectal temperature rose steadily until death. When molar sodium lactate was injected at hourly intervals and no glucose in water was administered, the cisternal pressure fell to subatmospheric levels (about –90 mm. saline solution) within 3 or 4 hours after the first injection.

The rate of excretion of water and salt in the urine increased following the injection of the hypertonic salt solutions. The increments of rate varied. The maximal rates of excretion of urine and sodium associated with the administration of the salt solutions are shown in Table II.

TABLE II

SOLUTION	MOLAR	MEAN URINE FLOW PER HOUR (FIRST HOUR AFTER INFUSION)	SODIUM EXCRETED (MEQ/HR.) (FIRST HOUR AFTER INFUSION)	CONCENTRATION OF SODIUM (MEQ/LITER URINE)
Sodium succinate	⅔	117 ml.	32	270
Sodium lactate	1	94	23	240
Sodium chloride	1	75	10	130
Glucose	2	96	—	—

DISCUSSION

These studies show that equiosmolar solutions of sodium succinate (⅔ molar), sodium lactate (molar), and sodium chloride (molar) are capable of consistently lowering cisternal pressure in anesthetized dogs. The reduction of cisternal pressure effected by any of the solutions is not significantly different from that produced by the others. This finding was unexpected because it was known that the rates of excretion of sodium and water attendant upon the injection of these salt solutions differed appreciably, as shown in Tables II and III. Before these experiments were performed we anticipated that sodium succinate would be more effective in lowering cisternal pressure than sodium lactate and that sodium lactate would be more effective than sodium chloride because the respective associated renal clearances of salt and water declined in that order.

Obviously, the rate of excretion of sodium and water attending the injection of the salt solutions had no appreciable effect upon the extent of the concomitant reduction of intracranial pressure. Furthermore, the reductions

of cisternal pressure effected by the different sodium salts were not correlatable with the changes in the volume of the calculated sodium space (see Table III).

TABLE III

SOLUTION	CHANGE IN CISTERNAL PRESSURE (MM. SALINE)	PER CENT VOLUME CHANGE OF SODIUM SPACE*	SODIUM EXCRETED / SODIUM INFUSED × 100 (PER CENT)
Sodium succinate	-120	-8.48	89
Sodium lactate	- 70	-4.84	55
Sodium chloride	-100	+4.24	27

*Sodium was assumed to have a volume of distribution that was identical with the extracellular fluid volume; the latter was taken to be 20 per cent of the control body weight of the dog. This volume represented sodium space 1. The control plasma sodium concentrations (Na 1) were determined, and Na space 1 × Na 1 = Total Na 1. A known amount of sodium was injected intravenously and the subsequent losses of sodium in the urine were determined; thus the new total sodium content (Total Na 2) was readily computed (Na 1 + Na injected less Na excreted = total Na 2). The new plasma sodium concentration (Na 2) was determined; then $\frac{\text{Total Na 2}}{\text{Concentration Na 2}}$ = Na space 2. The per cent change in sodium space = $\frac{\text{Na space 1 less Na space 2}}{\text{Na space 1}} \times 100$

It is also apparent that the characteristics of the anion have no influence upon the effectiveness of the salt in so far as intracranial pressure is concerned.

The volume of distribution* of the agent has great influence upon the change in intracranial pressure associated with its administration, as demonstrated by others.[5] Glucose and urea enter the cells of the body and therefore have a volume of distribution approaching that of the water in the body. Therefore, hypertonic solutions of glucose or urea reduce the pressure of the spinal fluid only temporarily. The secondary rise in intracranial pressure which follows the injection of hypertonic solutions of glucose and urea constitutes sufficient grounds for removing them from the list of substances used to reduce intracranial pressure. They are dangerous because they ultimately increase the pressure. Substances such as sucrose and salts of sodium which have a volume of distribution approximately equal to that of the extracellular water do not induce secondary rises in intracranial pressure when injected as hypertonic solutions therefore they are much safer than hypertonic solutions of glucose or urea. However, to inject them repeatedly is dangerous because their repetitive injection tends to be accompanied sooner or later by a steadily rising temperature and progressive hypotension.

Five and 10 per cent solutions of glucose in water when injected intravenously raise the intracranial pressure. The injection of only 7 ml. of 5 per cent glucose in water per kilogram of body weight practically doubled the

*The volume of distribution refers to the virtual volume of water in the body through which a given introduced substance becomes distributed in a concentration that is assumed to be identical with plasma concentration. Each substance has a characteristic volume of distribution which value has been determined for many solutes. For example sodium is in solution predominantly in extracellular fluid and the osmotic force of the injected sodium ion tends to move water only out of the cell. Glucose is distributed throughout extracellular and cellular fluids and the osmotic force of injected glucose tends to move water out of the cell only while its extracellular concentration is greater than its cellular concentration. Since the concentration gradient of glucose across the cellular membrane is soon abolished, the movement of water back into the cell occurs, the brain volume increases, and the intracranial pressure rises.

cisternal pressure of the animals used in this series of experiments. This action of glucose in water should constitute sufficient basis for its contraindication during the conduct of intracranial operations. For volume replacement of the fluids lost (except blood) during these operative procedures, an isotonic saline solution (Hartmann's solution) should be administered at a rate not to exceed 100 ml. per hour. If the operating room temperature is above 85° (F.) the rate of injection may be increased to approximate the rate of sweat losses. Cognizance is taken of the fact that in an individual who is operated upon a saline solution may not replace the pure water that is lost insensibly through the skin and lungs, and a moderate increase in osmolar concentration may ensue. This electrolyte aberration may, however, be more conducive to the recovery of the individual subjected to an intracranial operation than a normal ionic concentration. When 5 and 10 per cent solutions of glucose must be given to balance losses of water in the face of an increased intracranial pressure, they must be given very slowly and carefully.

Within the past 2 years ½, ⅔, and 1 molar solutions of racemic sodium lactate have been used in the hospitals of Dallas in attempts to reduce dangerous elevations of intracranial pressure and the swellings of the brain during craniotomy. Sodium lactate has proved to be useful in reducing brain swelling during intracranial operations and in reducing high intracranial pressures associated with subdural hematomas. It has not proved effective in altering the course of severe contusional brain injury.

Sodium succinate should not be employed clinically until more can be learned about it. The relatively large amounts of sodium retained after the administration of hypertonic sodium chloride make it theoretically less suitable than sodium lactate in the treatment of increased intracranial pressure. Whenever large amounts of hypertonic sodium lactate are given repeatedly the carbon dioxide combining capacity of the serum should be carefully followed so that alkalosis is not induced.

CONCLUSIONS

Equiosmolar solutions of sodium lactate, sodium succinate, and sodium chloride, when injected intravenously, reduce intracranial pressure without effecting significant secondary rises in pressure.

Hypertonic solutions of glucose (25 and 36 per cent), when injected intravenously, reduce the cisternal pressure only temporarily; the temporary reduction is followed by a rise in pressure to a height far above the preinjection level.

Seven milliliters of 5 per cent glucose in water per kilogram of body weight when administered intravenously practically double cisternal pressure.

Five and 10 per cent solutions of glucose in water should not be given during the course of intracranial operations. Fluid volume deficits should be replaced with an isotonic salt solution (Hartmann's solution).

The reductions in intracranial pressure effected by the various sodium salts are not correlatable with the renal clearances of sodium or water or with the concomitant changes in the volumes of sodium space.

Hypertonic glucose solutions should not be employed to reduce intracranial pressure because they ultimately induce a rise in pressure.

The repetitive administration of hypertonic sodium salts is potentially dangerous because progressive hyperpyrexia and hypotension are likely to attend it.

Hypertonic sodium lactate solutions are capable of reducing the herniation of the brain during craniotomy and of diminishing high spinal fluid pressures associated with subdural hematomas. They do not affect the course of severe contusional brain injuries.

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Case Reports

CAVERNOUS HEMANGIOMA OF THE PAROTID GLAND

Report of a Case

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CAVERNOUS hemangioma of the parotid gland occurs primarily in infants. In 30 cases reviewed by McFarland[2] in 1930 the oldest infant reported was 5 months of age. Glaser,[1] in 1946, added another case in a 2½-month-old child. There has been no report of a case of hemangioma of the parotid gland in a child or adult over 5 months of age. Since hemangioma of the parotid gland in the older child and in the adult is rare, report of a case of cavernous hemangioma of the parotid gland in a 15-year-old boy is presented.

R. A., a 15-year-old boy, was seen at the Colorado Springs Medical Center because of a "lump in the jaw" that had been present for 8 years. In recent months it had grown considerably in size. There was no history of trauma or history of the "lump" enlarging with eating or talking. The "lump" was aspirated by another physician and found to contain blood. Upon examination there was a soft, fixed mass about the size of a lemon which involved the right parotid gland and extended inferiorly to the angle of the right mandible. There was no discoloration of the skin or unusual enlargement of the vessels over the mass. There was no bruit.

The clinical diagnosis was a parotid tumor and surgical excision was advised. Under general anesthesia a total right parotidectomy was done on Aug. 9, 1949. The superficial and deep lobes were excised, and the facial nerve was carefully spared. The gland was unusually vascular. A diagnosis of cavernous hemangioma of the parotid gland was not made untl the pathologic study was completed.

The gross pathologic examination of the right parotid gland revealed a specimen measuring 5.0 cm. by 3.0 cm. by 2.0 cm. in dimension. The external surface contained irregular lobulations averaging 0.4 cm. in diameter. In addition to the lobulated tissue, a focal hemorrhagic section was observed. The microscopic examination of the sections revealed lobules of closely packed acini composed of angular, brightly basophilic cells with abundant, pale basophilic cytoplasm and polyhedral or ovoid basophilic nuclei. The lobues were separated by strands of fibrous connective tissue exhibiting hemorrhage and congestion (Fig. 1). In some fields a fibromuscular stroma was present in which there was extensive hemorrhage and necrosis and infiltration with plasma cells, lymphocytes, and polymorphonuclear cells. Closely packed, greatly dilated blood vessels were apparent in these areas (Fig. 2). Extensive desmoplastic reaction occurred in the areas of hemorrhage. The diagnosis was cavernous hemangioma of the right parotid gland.

The patient recovered rapidly from surgery with a minimum amount of residual scar. There was a temporary right facial nerve paresis due to operative trauma from which he had recovered completely 3 months after surgery (Fig. 3).

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*Diplomate American Board of Surgery.

Fig. 1.

Fig. 2.

Fig. 1.—The photomicrograph illustrates the lobules of parotid gland separated by strands of fibrous connective tissue, exhibiting hemorrhage, congestion, and large dilated blood vessels (×25).

Fig. 2.—The photomicrograph illustrates at lower power dilated, closely packed blood vessels typical of cavernous hemangioma (×10).

Cavernous hemangioma of the parotid gland undoubtedly is a congenital lesion. In this patient, the lesion was present at birth but did not become apparent until the eighth year of age. The hemangioma of the parotid gland is usually unilateral and often enlarges with crying or straining. The lesion is soft and compressible. The skin over the lesion may be normal or have a bluish discoloration typical of angiomatous or telangiectatic lesions. No signs of inflammation are found unless they have been complicated by infection. The tumor grows slowly at first but may suddenly increase in size until death results from invasion and compression of the vital structures. Invasion is usually by continuity with partial or total replacement of the parotid tissue, leaving the

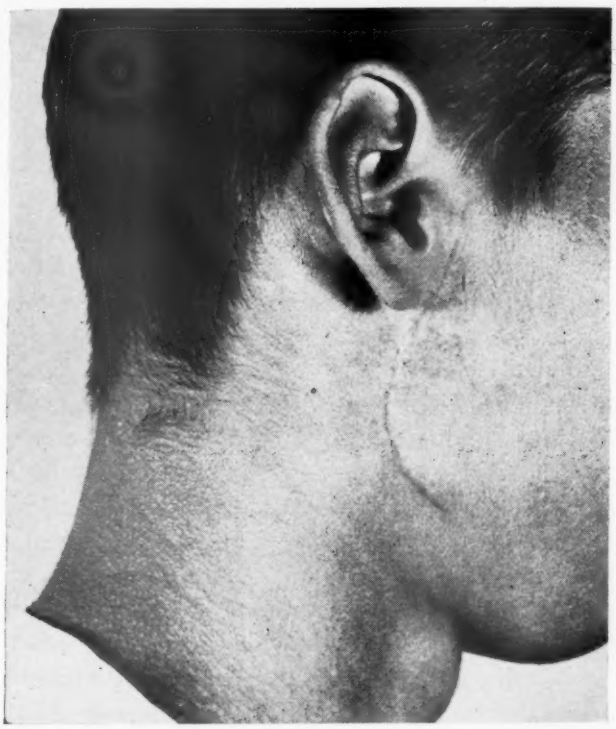

Fig. 3.—This illustrates the surgical scar and approach and result in excision of the parotid gland in the case presented.

ducts intact. The incidence is greater in the female than the male. The malignant clinical course of these lesions is not comparable to the benign macro- and microscopic appearance of the hemangioma which adds to the seriousness of the condition.

The treatment of angiomas of the parotid gland is surgical. Total extirpation of the gland including the superficial and deep lobes will avoid recurrences. The prognosis is excellent when total excision of the gland is done. Death may occur from rapid invasion of contiguous vital structures of the head and neck, usually following recurrences or inadequate excision of the lesion. Early excision will decrease morbidity and mortality.

CONCLUSION

1. A case of cavernous hemangioma of the parotid gland in a 15-year-old boy is presented.

2. The treatment is total excision of the gland with preservation of the facial nerve.

3. Death may occur from rapid invasion of contiguous vital structures of the head and neck, usually following inadequate excision of the lesion or lack of treatment.

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REMOVAL OF A PRIMARY LATERAL RETROPERITONEAL TERATOMA WITH SURVIVAL IN A FIFTEEN-HOUR-OLD INFANT

A Case Report

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THE purpose of this communication is to record the occurrence of a lateral retroperitoneal teratoma in a newborn infant. It was successfully removed 15 hours following birth.

According to a recent review by Palumbo and associates,[4] there were 57 "bona fide' cases of primary lateral retroperitoneal teratomas reported in the literature at the time of their survey. The youngest of these was in a neonatal infant whose exact age was not specified and the child died without surgery. The next youngest case was in a 7-week-old female infant in whom successful extirpation of the tumor was accomplished and reported by Lightwood.[3]

A discussion of the histologic and embryologic characteristics of this rather rare type tumor does not fall within the scope of this paper and the reader is referred to the excellent reviews by Palumbo and colleagues,[4] Hansmann and Budd,[2] and Arnheim.[1]

We feel that our case is noteworthy not only because the infant is apparently the youngest successfully treated patient on record, but it also demonstrates the development of these tumors in utero.

In addition, one cannot help but be impressed by the fact that surgery of this magnitude in newborn infants is possible by virtue of the advances in pre- and postoperative care. It is our opinion that in newborn infants presenting lesions which definitely require surgical therapy little is to be gained by procrastination. Delaying a necessary operative procedure in a newborn infant with the idea that time will better fit the infant for surgery is often fallacious, and, in fact, the reverse is often true: that is, he becomes a poorer operative risk. In this particular case in which the tumor was compromising the child's respirations and interfering with the portal circulation, delaying the operation would only serve to diminish the infant's ability to withstand the procedure.

CASE REPORT

History.—This white male infant was delivered spontaneously after a 40 week gestation of a para i, gravida ii mother. The total length of labor was 4½ hours and was uncomplicated. Maternal medication prior to delivery consisted of Demerol, 100 mg., and scopolamine, gr. 1/150, administered 45 minutes before the infant's birth. The baby breathed "sluggishly" following delivery, necessitating CO_2 and O_2 inhalation and tracheal aspiration.

The birth weight was 2,350 Gm. Respirations were very rapid and there was slight retraction of the ribs and intercostal spaces with inspiration and occasional coarse ronchi were heard in both lung fields on auscultation. The abdomen was protuberant and there

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was a palpable intra-abdominal mass which occupied almost the entire right half of the abdominal cavity. The skin over the abdomen was taut and glistening and many large, superficial, dilated veins were noted on the abdominal wall. The mass felt firm to hard in consistency, with a smooth surface and spherical contour. The remainder of the physical examination was essentially negative.

Laboratory Data.—The urine revealed a 2 plus albuminuria and was otherwise not remarkable. Hemoglobin was 12.5 Gm. per 100 c.c. and the red blood cell count was 4 million. The white blood cell count was 11,450, with 45 segmented neutrophils, 21 unsegmented neutrophils, 30 lymphocytes, 2 monocytes, 3 eosinophils, and 33 nucleated red blood cells per 100 white blood cells in the peripheral blood smear.

Fig. 1.—Roentgenogram of infant's abdomen showing focal calcification along lateral margin of tumor and displacement of intestines to the left by the neoplasm.

X-Ray Examination.—A flat plate of the infant's abdomen showed an irregular abdominal mass with focal calcification, filling most of the right side of the abdomen and displacing the intestine downward and forward (Fig. 1). A diagnosis of possible teratoma or neuroblastoma was suggested by the roentgenologist.

Operation.—The infant was taken to surgery 15 hours following birth and under satisfactory drop ether anesthesia a No. 20 cannula was introduced into a left ankle vein and a whole blood transfusion was started. The abdomen was prepared with green soap, saline solution, and tincture of Merthiolate, and draped. The peritoneal cavity was opened through a right rectus muscle splitting type incision. Upon entering the peritoneal cavity a small amount of clear yellow fluid escaped and the tumor mass presented into the wound. The

surface of the tumor was smooth, glistening, and brownish-red in color and covered by many tortuous dilated veins. The transverse colon was stretched across the anterior surface of the mass. The tumor was well-circumscribed with the exception of its posterior portion, which was attached to the retroperitoneal tissue superior to the upper pole of the right kidney; this area of attachment extended from the right lateral gutter to the vertebral column, displacing the duodenum medially. The tumor had displaced the liver and stomach cephalad and the intestines were occupying the left lower quadrant.

The transverse colon was dissected free from the tumor and retracted caudalward. The tumor was then freed from all surrounding structures with blunt dissection. At its retroperitoneal base several large vessels were noted entering the tumor. These were clamped, cut, and ligated, and the tumor removed in toto. Inspection and palpation of all abdominal viscera revealed no other abnormalities. The abdomen was then closed in layers, using fine silk sutures. The infant received 100 c.c. of whole blood during the course of the procedure and the immediate postoperative condition was good. The infant was placed in an incubator following surgery.

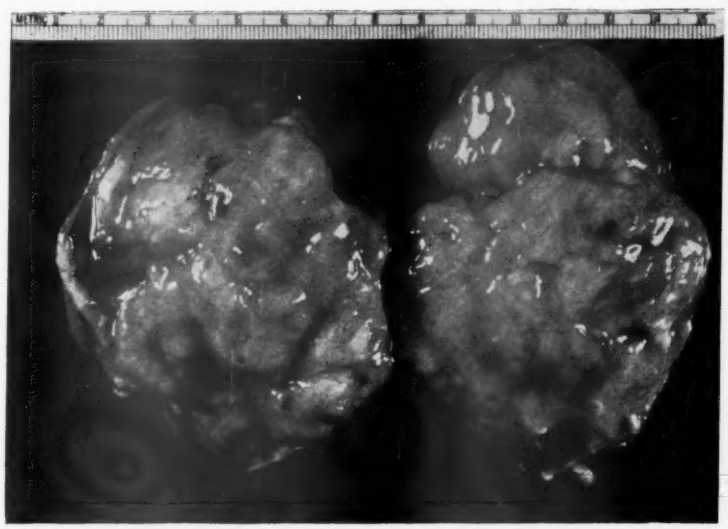

Fig. 2.—Cross-sectional view of teratoma showing moist, gelatinous cut surface and small cysts within the tumor tissue.

Pathologic Description.—The tumor measured 9 by 8 by 7 cm. and weighed 210 Gm. The external surface was reddish-gray mottled with brown and roughened by fibrous tags. The cut surface of the tissue was soft, yellow in color, and moist and gelatinous in consistency with the exception of focal calcification. There were occasional small cysts scattered throughout the tissue, the largest of which measured 1 cm. in diameter and contained thin, clear fluid (Fig. 2). Microscopically the tumor possessed a markedly varied appearance. The stroma was composed of loosely arranged cells having fibrillar or clear cytoplasm and round or oval normal chromatic nuclei. Within the matrix were round nodules of cartilage, large and small acini of one to three layers of cuboidal or columnar epithelium. Some of these acini resembled those seen in endometrium and others resembled salivary gland tissue. In some sections there were markedly irregular spaces lined by a single layer of flat or low cuboidal epithelium. Occasionally within these spaces the cuboidal epithelium formed irregular branching papillae. These papillae had a fibrovascular core. In one or two sections the stroma was moderately dense, hyalinized, and calcified. None of the tissue elements showed evidence of malignancy.

Diagnosis.—The pathologic diagnosis was teratoma of retroperitoneal space.

Hospital Course.—Postoperatively the infant's daily fluid and caloric requirements were met with parental fluids. Oral feedings of small quantities of 5 per cent Karo syrup

solution were begun on the second postoperative day. These were tolerated only moderately well in that there was occasional vomiting. Gavage feedings were then instituted with more gratifying results. The diet was increased progressively during the patient's hospital stay and the infant showed a weight gain of 810 Gm. over the birth weight at the time of discharge on the sixty-third postoperative day. Follow-up studies in the Out-Patient Clinic revealed progressive weight gain and normal development 6 months following surgery.

SUMMARY

A case of a primary lateral retroperitoneal teratoma in a newborn infant is reported. Successful surgical removal was accomplished 15 hours following birth of the infant.

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CAROTID BODY TUMOR IN A PATIENT WITH EPILEPSY

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DURING the 70 year span since the first removal of a carotid body tumor by Riegner (1880), less than 300 cases have been recorded in the medical literature. It is the purpose of this presentation to review briefly the pertinent features in the management of tumors of the carotid body and to report the first instance, so far as can be determined, of a tumor of the carotid body occurring in a patient with epilepsy.

The first description of a carotid body is credited to von Haller in 1743. The normal carotid body is an ovoid, encapsulated, 5 by 3 by 2 mm. sized, grayish-brown or reddish colored mass, located at or near (usually directly behind) each common carotid artery bifurcation. Nutrient vessels traverse a fibrous band, the ligament of Mayer, which joins the carotid body to the carotid bifurcation. The nerve supply consists of fibers from the descending branch of the glossopharyngeal nerve (the carotid sinus nerve of Hering), the superior cervical sympathetic ganglion, the vagus nerve, and the hypoglossal nerve. Microscopic examination of the carotid body reveals large polygonal, pale-staining, parenchymal cells, with finely granular cytoplasm, containing oval or round, eccentric, hyperchromatic nuclei. A few of the cells exhibit granules which display an affinity for chrome salts, and, by virtue of this characteristic some observes have placed the carotid bodies in the chromaffin system.

Although the exact function of the carotid body has not been established, it is known that bilateral removal of these structures can be performed without untoward sequelae. The concept of an endocrine function, once vigorously supported, has now been abandoned.[1] Dripps and Comroe,[2] as a result of extensive experiments, concluded that both the carotid and aortic bodies are chemoreceptors, stimulated by changes in the composition of arterial blood, and exerting effects on respiration which are contrary to those initiated by the pressoreceptors located in the carotid sinus and in the arch of the aorta. It is noteworthy that the association of a carotid body tumor with the carotid sinus syndrome is very infrequent.[3]

Pathologic change in the carotid body is limited to tumor formation.[4] Various terms, including perithelioma, paraganglioma, neuroblastoma, and endothelioma, have been used to designate carotid body tumor. Reid[5] suggested that either the term "hyperplasia" or "adenoma" was appropriate. The shape, encapsulation, and lobulation of the normal carotid body are reflected in the tumor, which is characteristically slow-growing, compressible, and varies in size from that of a hazelnut to a goose egg, with the cut surface of a reddish-gray or purplish-brown hue. Although carotid body tumors are almost always unilateral, several instances of bilateral tumors have been reported.[6]

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Harrington, Clagett, and Dockerty[7] distinguished 2 cellular patterns; "alveolar" and "peritheliomatous," with at times a mixture of these 2 types. The former is characterized by large groups of pale polyhedral cells, with scanty connective tissue and little, if any, hyalinization. In the peritheliomatous pattern, the cellular units are smaller, more irregular, with a vascular and very dense connective tissue which exhibits marked hyalinization.

Definite malignancy, as revealed by cellular variation, active mitosis, and invasion of the capsule, is present in a varying percentage, according to different authors. In each of the series of cases reported by Rankin and Wellbrock,[8] Harrington, Clagett, and Dockerty,[7] and MacComb,[9] the incidence of malignancy was recorded as 50 per cent, whereas in the group of 18 cases reported by Lahey and Warren[10] there was no proved malignant tumor. Gratiot,[11] after an extensive review, estimated that probably 15 to 20 per cent of carotid body tumors do become malignant.

Most commonly, the presence of a mass in the upper anterolateral cervical region is the only evidence of a carotid body tumor. An average time interval of 6 years elapses before the patient consults the physician regarding this swelling. Symptoms, when they do occur, are the result of pressure of the tumor upon adjacent structures, that is, the recurrent laryngeal, sympathetic, and vagus nerves, and the esophagus and pharynx. The tumor must be differentiated from carotid aneurysm, branchial cyst, neurofibroma, metastatic carcinoma, aberrant thyroid, branchiogenic carcinoma, and cervical adenopathy, among other pathologic entities. Aspiration by the punch technique has been recommended by some to secure a specimen for examination, but this appears to be a very hazardous procedure, and the pathologic study by this method is subject to considerable error. All of the collective reviews recorded in the literature attest to the fact that rarely is a preoperative diagnosis made. A diagnosis prior to operation is facilitated if one bears in mind the possibility of a carotid body tumor whenever there is encountered a painless, slow-growing mass in the superior, anterior cervical triangle, exhibiting lateral without vertical mobility, and which, upon digital compression, promptly decreases in size, only to slowly regain its original dimensions upon release of pressure. The tumor is usually deep seated and is never attached to the skin. Although rarely a bruit or thrill may be elicited, this is not common.

CASE REPORT

This 26-year-old white soldier was admitted to Walter Reed General Hospital, Army Medical Center, Washington, D. C., with a diagnosis of epilepsy, grand mal. Nine months previously, during a fall from a truck, the patient sustained a severe blow to his head without loss of consciousness. Three months prior to admission he experienced for the first time a convulsive seizure, and subsequent seizures occurred at the rate of approximately 2 per month. Also, the patient had noted a mass on the left side of his neck, just below the angle of the mandible, for a period of 2½ months prior to admission. A gradual increase in the size of the mass had occurred.

Physical examination was essentially negative, aside from the presence of a 2½ cm. sized, discrete mass, located in the left anterolateral cervical region below the angle of the mandible. There was no attachment to the overlying skin, and the mass was reported as slightly movable. Laboratory studies, including complete blood count, urinalysis, and fasting

blood sugar, were all within normal limits. Complete neurologic examination was negative, and the electroencephalogram revealed a pattern consistent with grand mal type of epilepsy. Customary therapy was directed toward regulation of the epileptic state.

A preoperative diagnosis of branchial cyst was made, and exploration of the region performed through an oblique incision, under gas-oxygen-ether anesthesia. An ovoid, firm but elastic, reddish-brown colored tumor mass, partially encircling the region of the bifurcation of the common carotid artery, was found. Marked decrease in size of the mass resulted from compression, and a slow return to normal size occurred following release of compression. Since the tumor mass was inseparably related to the carotid bifurcation, sacrifice of the great carotid vessels would have been necessary to accomplish complete removal of what was considered a carotid body tumor. Accordingly, the procedure was terminated so that further investigation and observation might be accomplished.

The patient's condition following operation remained unchanged, and therapy designed to control the epilepsy was continued. The possible relationship of the tumor mass and the epilepsy was an intriguing one. Repeated tests revealed no evidence of hypersensitivity of

Fig. 1.—Arteriogram showing the diffusion of radiopaque solution into the carotid body tumor, which appears to be centered over the external carotid artery just distal to the bifurcation of the common carotid.

the carotid sinus. The use of sodium cyanide intravenously for carotid body sensitivity showed a full respiratory response. Repeat neurologic examination was entirely negative. The patient was then observed at intervals over a period of 3 months, and it was apparent that the tumor was slowly increasing in size. Since this was true, operative removal of the carotid body tumor was deemed advisable and, in preparation for the procedure, manual compression of the common carotid artery against the anterior tubercle of the left sixth transverse process was accomplished daily for a period of several weeks prior to operation in an effort to promote collateral cerebral circulation. A plan of operative management, similar to that employed by the neurosurgical section in the treatment of intracranial aneurysms, was adopted.

At the first stage operation, performed under local (procaine) anesthesia, in July, 1947, an incision was made anterior and parallel to the left sternocleidomastoid muscle. The carotid sheath was opened, the internal jugular vein retracted laterally, and the common carotid artery isolated. An arterial clamp was gently closed upon the carotid, producing complete occlusion which was maintained over a period of 20 minutes, during which interval repeated careful neurologic examination failed to reveal any abnormality. The patient was then transferred to the x-ray department where an arteriogram was done, using Diodrast solution

(Fig. 1). The injection of this radiopaque solution resulted in a transient aphasia, which cleared rapidly. The patient was then returned to the operating room, where ligation and division of the common carotid artery was performed. The postoperative course was uneventful.

One week later, the patient was reoperated upon, again under procaine infiltration anesthesia. The orginal incision was opened and extended (Fig. 2), and the distal stump of the common carotid artery, together with the tumor mass (which was fused to the bifurcation of the common carotid artery), was mobilized. The cervical sympathetic trunk and the vagus nerve were both densely adherent to the lateral aspect of the tumor, but careful dissection resulted in the separation of these structures. The internal carotid artery was then temporarily occluded by the use of an arterial clamp for a period of 20 minutes without untoward effect. Subsequently, the tumor and adjacent sections of common carotid, internal carotid, and external carotid vessels were resected en masse. The integrity of the cervical sympathetic plexus and the vagus and hypoglossal nerves was preserved.

Fig. 2.—Photograph one week after operation illustrating the incision employed for removal of carotid body tumor, together with resection of the great carotid vessels.

Pathologic Report.—

Gross specimen: The specimen consisted of a firm mass, measuring 3 cm. in diameter, intimately fused to the region of the bifurcation of the common carotid artery and the adjacent sections of internal and external carotid arteries. The mass was partially covered by muscle and connective tissue. Within the common carotid there was a thrombus, measuring 2 cm. in length and extending up to and including a portion of the lumen of the bifurcation.

Microscopic study: Sections of the tumor adjacent to the carotid vessels presented an oval, lobulated neoplasm, which appeared to be completely surrounded by a dense intact capsule. The tumor was composed of rather closely-packed, pale cells, exhibiting plump, pale, finely granular to vacuolated, eosinophilic cytoplasm, and large, oval to round hyperchromatic and vesicular nuclei, which, for the most part, were rather uniform and which rarely showed mitoses. These cells were arranged in small, oval to round nests of 10 to 15

cells, each nest being surrounded by a thick membrane (Fig. 3). The cells in some areas were arranged to form well-defined alveoli having a central vacuolated space, which occasionally contained a small amount of secretion. Vascular spaces were frequently seen throughout the delicate perialveolar connective tissue, and dense hyalinized connective tissue stroma produced a fairly well-defined lobulation with occasional areas of distortion (Fig. 4). There was no evidence of true capsular infiltration.

Diagnosis.—The diagnosis was carotid body tumor.

The patient experienced a smooth postoperative course. Careful neurologic examination revealed slight difficulty in speech and mild loss of memory for recent events, in addition to a mild peripheral left facial weakness. However, these abnormal findings all cleared within the next few weeks. Electroencephalograms demonstrated no essential change from the pattern observed prior to the operative procedure. Timely anticoagulant therapy would have been appropriate in this case to minimize the tendency to thrombus formation.

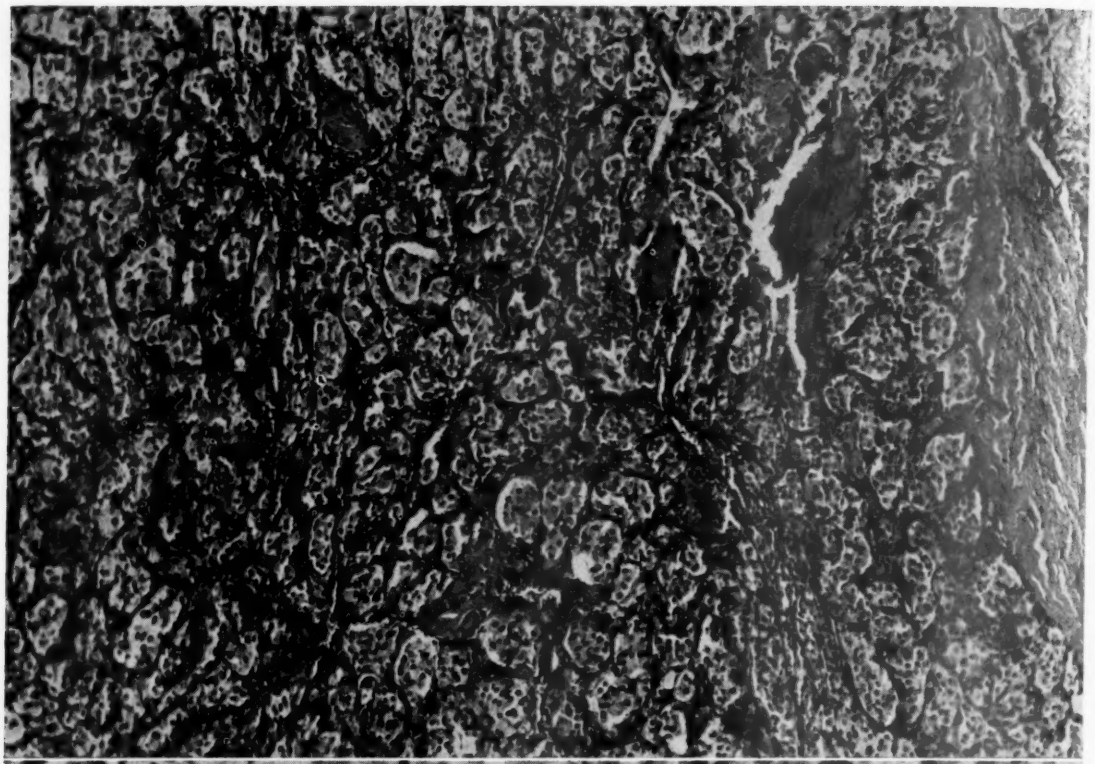
Other than the transient effects just noted, there were no unfavorable sequelae incident to the surgical removal of the carotid body tumor and sacrifice of the carotid vessels in this particular case. Three and one-half years have now elapsed since operation, and the patient remains in excellent condition aside from epilepsy, the status of which is unchanged.

TREATMENT

Ideally, complete surgical removal of tumors of the carotid body is the treatment of choice. The attempt to attain this ideal, however, must be tempered with the knowledge of the high mortality and morbidity attendant upon sacrifice of the great carotid vessels. Harrington, Clagett, and Dockerty found ligation of the carotid vessels necessary in 9 of 19 cases. Lahey and Warren, in order to extirpate the carotid body tumor completely, sectioned the carotid vessels in 6 out of a total of 18 cases. MacComb reported a series of 10 cases at the Memorial Hospital in New York of which division of the carotids was necessary in 7 patients. Considering only those cases in which sacrifice of the carotid vessels was necessary, the following mortality rates are highly significant: Harrington, Clagett, and Dockerty, 44 per cent; Lahey and Warren, 33 per cent; MacComb, 57 per cent. Peterson and Meeker[12] emphasized that not only is mortality a factor, but the relatively high morbidity rate must be considered. These authors reported a morbidity of 83.3 per cent, and this figure represents the incidence of those patients suffering from all degrees of disability, both transient and permanent. The report by Bevan and McCarthy[19] of a "cure" of a carotid body tumor by x-ray treatment has not been duplicated by others. Radiation therapy appears to have little, if any, beneficial effect.

There is complete agreement on the principle of extirpation of the growth in those cases wherein this can be accomplished with preservation of the integrity of the great carotid vessels.[11, 13-17] Opinions differs widely, however, as to the proper management of those cases requiring section of the carotid vessels. Some surgeons[7, 18] believe that all carotid body tumors should be removed regardless of the necessity of inclusion of the carotid vessels. Others[10, 15, 19] strongly recommend that ablation of carotid body tumors should not be accomplished where division of the carotid vessels is necessary, except in those cases exhibiting unequivocal evidence of malignancy or profound pressure effects, such as marked dysphagia. Manual compression of the common carotid artery against the prominent anterior tubercle of the sixth cervical vertebra has been recommended[7]

Fig. 3.



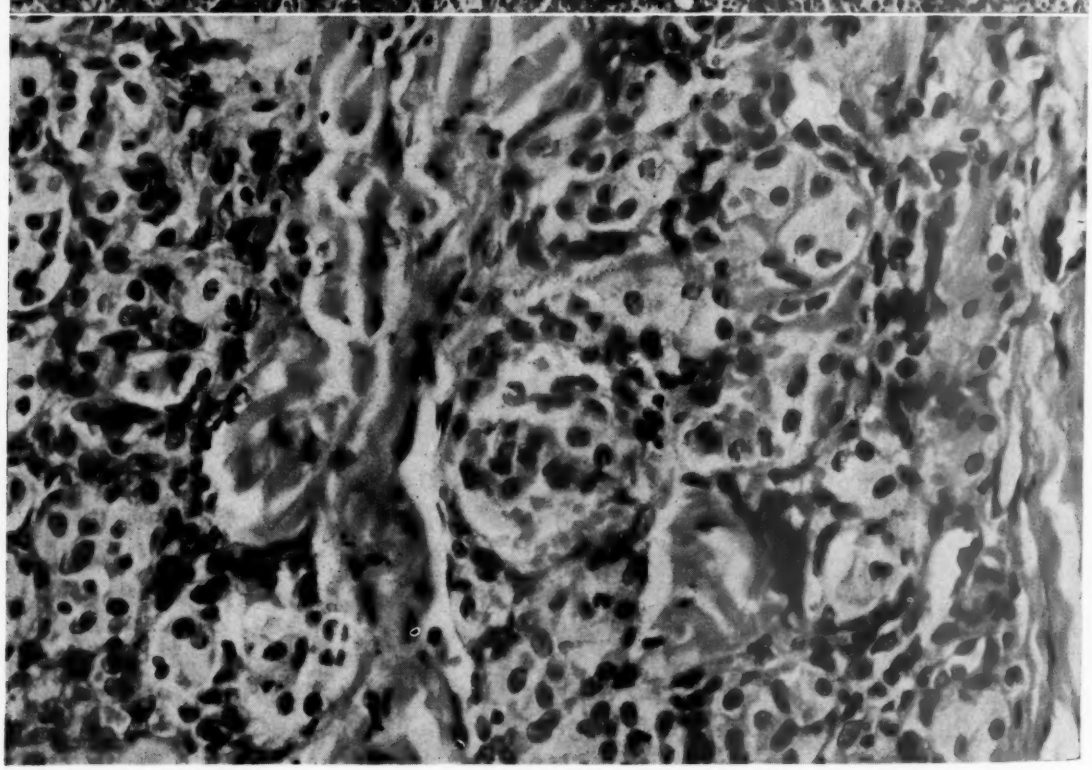


Fig. 4.

Fig. 3.—Photomicrograph. Note the arrangement of the cellular groups into nests and strands. In some areas, alveolar units are separated by numerous vascular spaces (Neg. No. 103240 Army Institute of Pathology, ×100).

Fig. 4.—Photomicrograph, demonstrating the rather large polyhedral cells with hyperchromatic nuclei. Hyalinization of the connective tissue is a prominent feature (Neg. No. 103241 Army Institute of Pathology, ×435).

as a means designed to promote the development of anastomotic cerebral circulation. Perhaps the most practical, although not infallible, method of determining the adequacy of the collateral cerebral circulation consists in the complete occlusion of the common carotid or internal carotid artery for 20 to 40 minutes while the patient is under local anesthesia. This serves well as an important preliminary step to actual ligation. Stage operations, as a possible answer to the problem of management, have been proposed. Gradual occlusion of the common carotid artery, by one of the several ingenious devices which have been used for that purpose, may be performed,[9, 11, 20] with resection of the tumor and attached vessels at a subsequent stage. Another approach, developed by Poppen in the treatment of intracranial aneurysms, and described by Lahey, is the low ligation of the common carotid artery by an infolding technique, producing less trauma to the vessel wall, and thus reducing the possibility of thrombus formation. Immediate heparinization of the patient is instituted with reoperation 6 weeks later.

Neurologic complications, including death, hemiplegia, and lesser effects, result most commonly from inadequate collateral circulation to the brain, ascending thrombosis of the internal carotid artery, and emboli detached from mural thrombi at the site of division of the carotid artery. To minimize the incidence of these complications, cervical sympathetic block with procaine and the use of papaverine are of value.[21] Although the use of anticoagulant therapy has received relatively scant attention[9, 16, 21] even in recent years, yet to employ this therapeutic adjunct immediately following ligation or division of the great carotid vessels appears sound.

SUMMARY

Salient characteristics of the carotid body are reviewed and the pathologic and clinical features of carotid body tumors are discussed. Although the proper management of carotid body tumors has been the subject of considerable debate, it would appear that, in view of the distressing mortality and morbidity, a more conservative approach is advisable. The successful surgical removal of a carotid body tumor occurring in a patient with epilepsy is reported.

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HEMANGIOENDOTHELIOMA OF THE STOMACH

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INTEREST in polypoid lesions of the stomach has been greatly stimulated by the recent work of Wise[1] and Pearl and Brunn.[2, 3] The case herein reported is presented because the specimen, a hemangioendothelioma of the stomach, is a pathologic curiosity, and the patient, a 90-year-old man, withstood subtotal gastric resection and has remained in good health for 2½ years subsequent to the performance of this procedure.

CASE REPORT

A 90-year-old man was admitted to Presbyterian Hospital on May 24, 1948. He complained of anorexia and vomiting. Two weeks before hospital admission he was awakened from a sound sleep by a severe episode of coughing. This was followed by a sensation of epigastric fullness and vomiting. The patient continued to vomit and stated that he had no desire for food. The vomitus consisted of clear fluid and undigested fragments of any food that he had attempted to eat. The recent and remote history was noncontributory. The patient had gradually lost 25 pounds of weight over a 20 year period.

The admission physical examination was negative except for dehydration. The blood count and urinalysis were within normal limits. An upper gastrointestinal tract roentgenogram revealed the presence of a constricting lesion of the lower end of the stomach which reduced its lumen to an estimated diameter of 2.5 mm. (Fig. 1).

An electrocardiogram recorded on the day of the hospital admission demonstrated incomplete bundle branch block. On June 1, 1948, a subtotal gastric resection was accomplished under gas-oxygen-ether anesthesia. Gastrointestinal continuity was re-established with a Hofmeister modification of the posterior Pólya type of anastomosis.

The pathologist reported the following:

Macroscopic Examination.—The stomach measured 9 cm. along its lesser curvature and 16 cm. along its greater curvature (Fig. 2). The stomach was opened along its lesser curvature, revealing a meaty, polypoid structure, 4 to 4.5 cm. in diameter, attached to the anterior wall of the stomach, estimated to be midway between the lesser and greater curvature. This polyp was present 4 cm. proximal to the distally resected segment and was attached by a pedicle, 2.5 cm. long and 1 to 1.5 cm. in diameter, which appeared to consist of pulled up mucosa and submucosa. The wall opposite this attachment was moderately indurated and somewhat thickened, with this thickening being apparent on the serosal surface. The polypoid structure presented eroded mucosal surface over its fundus, and here it was covered by a light yellowish-brown substance. Sections revealed the greater part of the pedicle to consist of mucinous type semicartilaginous tissue which crunched on pressure. Definite tumor was not observed in the stalk (3 sections polyp, 2 sections pedicle, 1 section including pedicle from serosal surface in that area of induration).

Microscopic Examination.—Sections revealed ulceration of the mucosa over the fundus (Fig. 3). The tumor consisted of clusters of angiomatous elements in fibroconnective tissue which was loose and presented groups of endothelial-type cells. The major element of the tumor was composed of concentrically arranged endothelial-type cells which were spindle shaped and appeared to originate from a generally small, centrally placed capillary which was an intrinsic part of the lesion. The over-all picture may be best described as an "onion peel" arrangement. It resembled in many aspects the glomus body, giving one

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Fig. 1.—Roentgenogram of the patient's stomach.

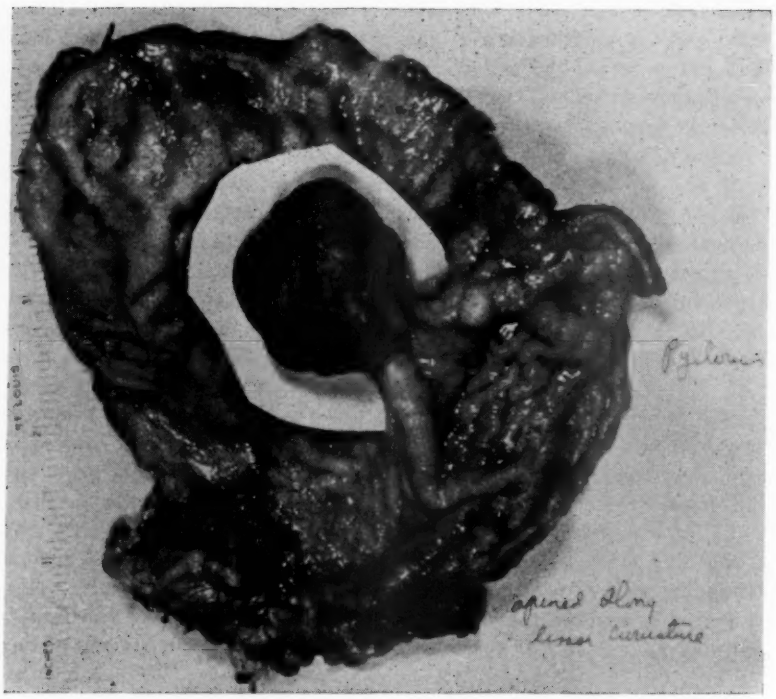

Fig. 2.—Photograph of resected stomach.

the feeling that this lesion was of both nerve and vascular origin. The tumor was not encapsulated and not too well demarcated. The stroma was heavily infiltrated with round cells and eosinophiles.

Diagnosis.—The diagnosis was hemangioendothelioma, polypoid and pedunculated, of the stomach.

The patient's postoperative course was complicated by mild cardiac decompensation from excessive parenteral fluid administration. This was controlled with digitalis. The patient was discharged from the hospital on the twenty-first postoperative day. He has maintained normal nutritional status since operation.

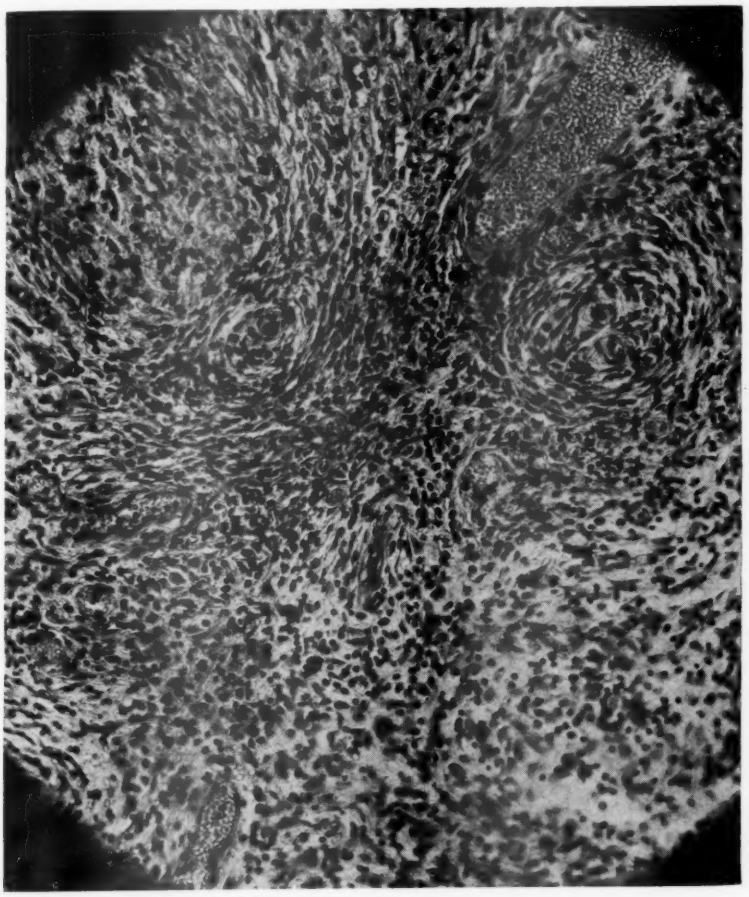

Fig. 3.—Photomicrograph showing histologic appearance of tumor.

COMMENT

The literature pertinent to hemangioendothelioma has been recently reviewed by Legg and Fitch.[4] They added 2 cases, one occurring in the soft tissue of the neck and the other in the lower one-third of the right tibia. Jaffee[5] discussed the pathology of vascular tumors falling into this category and collected the following combinations of sites for their occurrence from the literature: skin, liver, spleen, and bones of the skull (Billroth[6]); involvement of the base of the skull, the bone marrow, and the urinary bladder (Brandt[7]); skin, liver, parotid gland, and intestine (Gascoyen[8]); skin, mucous membranes, mesentery,

and retroperitoneal tissue (Ghon[9]); skin and pia mater (Kalischer[10]); liver and bones of the skull (Major and Black[11]); liver, suprarenal gland, ovaries, and uterus (Payne[12]); skin, mucous membranes, liver and heart (Runge[13]); cerebellum, medulla oblongata, spinal cord, liver, and urinary bladder (Tanneberg[14]); skin and internal organs (Von Topfer[15]). He added a case of multiple hemangiomata involving the skin leptomeninges, anterior roots of the cervical nerves, pia mater spinalis, the diploë of the parietal bone, the thyroid, the lungs, the intestines, and the spleen. In this rather exhaustive review he was unable to find a case report of a hemangioendothelioma or similar vascular tumor involving the stomach either primarily or secondarily. Subsequent to this work we were able to find 1 angiosarcoma reported by D'Aunoy and Zoeller[16] in a review of 135 cases of sarcoma of the stomach and 2 cases reported by Lemon & Broders[17] encountered at the Mayo Clinic between 1908 and 1938.

Another phase that warrants some emphasis is the age of this patient. The circumstances subsequent to the surgical procedure in this instance were directly opposite to the experience one of Wangensteen's[18] associates had with a geriatric case. "When this procedure had been successfully completed nobody wanted the poor fellow, and the only alternative for the surgeon appeared to be to take the patient home with him." In contrast the 93-year-old patient whose history is recorded here works steadily, he and his wife have enjoyed 2 seasons of trout fishing in the mountain streams, and he is living a very independent life at the present time.

SUMMARY

The literature on hemangioendothelioma has been reviewed. An additional case in which the tumor involved the stomach is added to the literature.

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EOSINOPHILIC GRANULOMA OF THE STOMACH AND SMALL INTESTINE

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HERRERA and Guardia[1] presented the first extensive description and exhaustive case study of this granulomatous lesion occurring in the gastrointestinal tract. In March, 1948, they reported the case of a 55-year-old man with a 2-month history of postprandial pain, nausea, and vomiting, the latter relieving the epigastric pain. There was a preceding history of vague gastric complaints of many years' duration. A radiographic diagnosis of pyloric obstruction was made and surgical exploration revealed marked "thickening of the pylorus in tumor form." The tumor process was yellow-green in color and in consistency it was very soft and friable. Along the entire length of the small bowel there were bands of annular thickening of the same yellow-green color which, during peristaltic activity, were converted into "knotty tumors." The entire process was confined to the pylorus, duodenum, and small intestine, ending abruptly at the cecum and without any evidence of mesenteric adenopathy. A subtotal gastrectomy was performed, and, because the lesion was considered inflammatory, postoperative penicillin was given. An unusual postoperative observation was an early, marked polymorphonuclear leucocytosis which, as it subsided, was attended by a gradual increase of eosinophils, a 20 per cent eosinophilia being present on the seventh postoperative day. The specimen presented normal mucosa but the wall of the pylorus measured 2.5 cm. thick. The marked eosinophil response was in the muscularis, and to a lesser extent in the submucosa.

Barrie and Anderson,[2] also in 1948, described a lesion in the pyloric antrum which they felt was an unusual organic change caused by an allergic reaction. They presented the case of a 27-year-old woman for whom gastric resection was done because of pyloric obstruction which was found to be due to both a concentric hypertrophy of the muscular coat of the stomach, pylorus, and duodenum, and a massive eosinophilic infiltration of the pylorus associated with peculiar pararterial giant-cell follicles. They suggested that this was an example of a true organic intestinal allergic reaction in so far as the patient had a specific intolerance to certain foods and had a constant blood eosinophilia associated with the localized tissue eosinophilia of the pylorus.

Vanek,[3] in 1949, presented 6 cases of submucosal granuloma with eosinophilic infiltration occurring in the stomach and summarized the histologic features as those of a basophilic connective tissue reaction composed of fibroblasts or fibrocytes and loosely arranged collagenous fibers, with an infiltration of eosinophilic leucocytes and lymphocytes, the latter being occasionally

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accumulated in rudimentray lymph follicles, and, third, a marked proliferation of arterioles and capillaries and dilated lymphatic vessels. He especially noted that the borders of this lesion were ill-defined and there was no tendency to encapsulation. The mucous membrane covering the tissue was thinned out and the lesion did not infiltrate through the muscularis mucosae, though it occasionally did penetrate it and reach the mucosa. The 6 patients that he presented showed various types of clinical manifestations.

More recently Polayes and Krieger[4] have described this same lesion, occurring in the jejunum, and simulating a malignant neoplasm causing intestinal obstruction. A small bowel resection was followed by an uneventful postoperative course. These authors cited Stout's experience with a gastric lesion of this type which occurred in a stomach removed for gastric ulcer.

In reviewing the cases reported (Table I) it is apparent that the most common manifestation of the disease is the formation of a poorly circumscribed submucosal nodule which tends to become pedunculated and polypoid, and which occurs most frequently in the pyloric antrum. However, the pyloric sphincter does not seem to be the limit of the extension in a few cases. Because of the comparative rarity of the disease and because its various manifestations have not been integrated in surgical consideration, we wish to report a rather early eosinophilic granuloma of the stomach which was also unique because of the syndrome it presented by intermittently prolapsing through the pylorus. A preoperative diagnosis of prolapsing polyp of the pylorus was made, a rather unusual lesion in itself in so far as the incidence of prolapsing tumors of the stomach is considered to be a fraction of 1 per cent of the new growths in that organ.[5]

CASE REPORT

E. B., a 57-year-old woman, was first seen in the Gastric Clinic of The Memorial Hospital on April 26, 1950, having been referred by her physician with radiographs which had been interpreted as showing a polyp of the duodenum.

The present illness had begun 6 months previously, at which time she first noticed a localized epigastric burning which came on from 30 to 60 minutes after a meal and which would last from one-half to one hour. It was relieved by lying down or by drinking cold water, but was not affected by milk or antacids. There had been no vomiting or nausea and no radiation of the pain. She stated that she had had a duodenal ulcer diagnosed by x-ray study 5 years before, and at that time she had had symptoms similar to those of her present complaint except that the interval between eating food and onset of symptoms was 2 to 3 hours. At that time she was relieved by food, milk, or an alkali. With dietary medication and antispasmodics she was relieved. Three years before onset of the present illness she again had pain in the right upper quadrant, with, however, nausea and vomiting. This occurred immediately after eating and at that time a gastrointestinal series showed that the previous ulcer had healed.

The patient's past history revealed that she had been treated in the hospital in 1948 for vesicle trigonitis and that she had had a lipoma removed from the subcutaneous tissues of the shoulder. She stated that she knew she had hypertension and that she had the occasional symptom of pounding in the head during excitement, but otherwise it caused her no trouble. She stated that a tumor which had been diagnosed as Weber-Christian disease had been removed from the left popliteal space in 1947.

There was no significant history in the family except that one sister had been said to have "rose fever."

TABLE I. EOSINOPHILIC GRANULOMA OF STOMACH AND SMALL INTESTINE

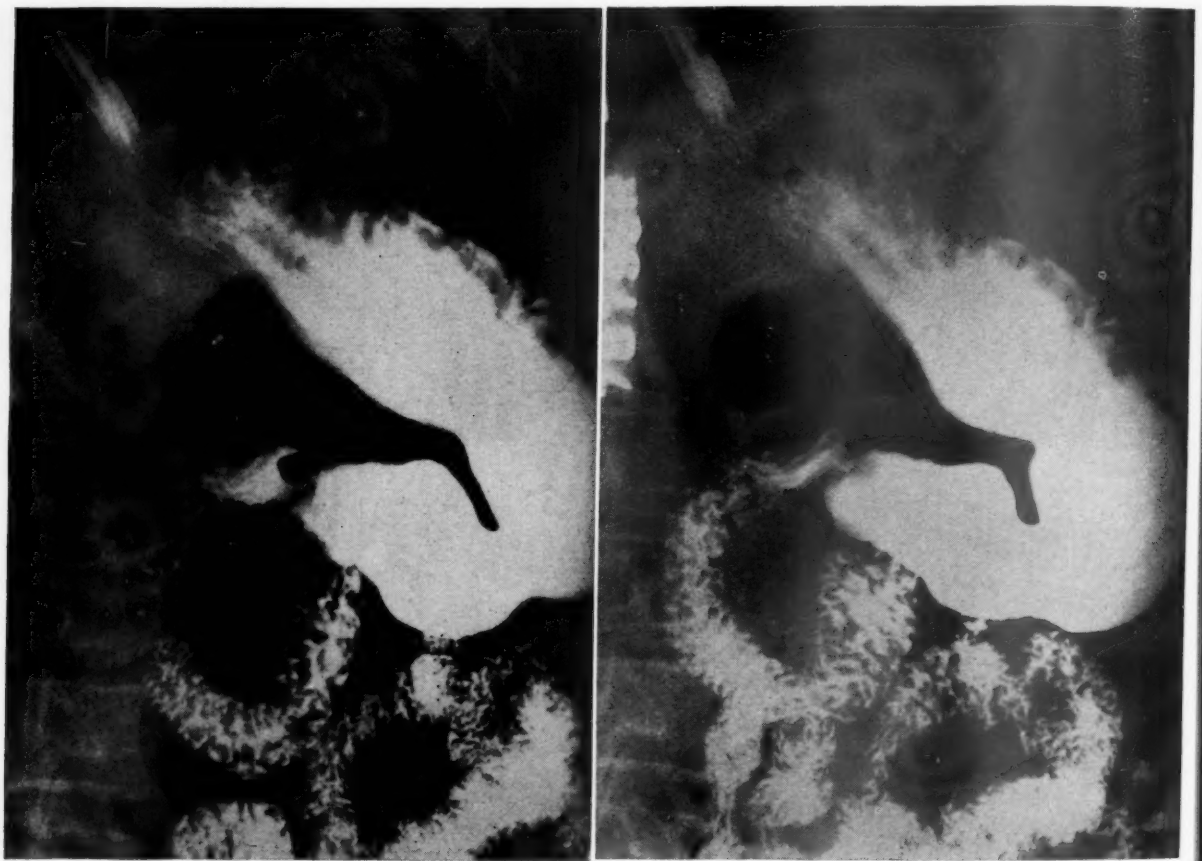
AUTHOR AND YEAR	SEX AND AGE	SYMPTOMATOLOGY AND DURATION	X-RAY FINDINGS	EOSINOPHILS PER C. MM.	HISTORY OF ALLERGY	TREATMENT	GROSS ANATOMY
1. Herrera and Guardia, 1948	Male 55	Epigastric, postprandial pain, nausea, and vomiting, which alleviated pain, 2 months; vague gastric disturbances for many years	Obstructing pyloric lesion	Preoperative normal; seventh postoperative day, 1,740		Partial gastrectomy	Marked thickening of pylorus, yellowish-green in color, and with bandlike thickenings of small bowel of same color
2. Barrie and Anderson, 1948	Female 27	Constant circumumbilical pain, retrosternal pain relieved by vomiting	Smooth prepyloric filling defect of greater curvature	Preoperative, 3,060; 3 weeks postoperatively, 3,658	Possibly	Partial gastrectomy	Pylorus, duodenum, and first 2 feet of jejunum were greatly thickened; mucosa was intact but submucosa was thickened
3. Vanek, 1949	Male 46	Symptoms of pyloric stenosis; loss of weight	Pyloric stenosis with thickening of mucosa		No	Partial gastrectomy	In submucosa there was a plum-sized, grayish-white, soft, ill-defined nodule
4. Vanek, 1949	Female 64	Pain beneath xiphoid which disappeared at rest, 6 months; loss of weight	Prepyloric tumor		No	Partial gastrectomy	Polyp on a long stalk, of brownish-violet color; lesion about 2 cm. above pylorus
5. Vanek, 1949	Male 55	Indefinite pressure in epigastrium, especially when stomach was empty, 20 years; diagnosis of gastric ulcer	Prepyloric tumor	78	No	Gastric resection	Small polyp 2 cm. above pylorus

6. Vanek, 1949	Male 57	Burning and epigastric pain, 3 years; vomiting, 7 weeks	Pyloric stenosis	93	No	Gastric resection	Grayish-white, sharply-defined, pea sized nodule at side of deep gastric ulcer crater
7. Vanek, 1949	Female 56	Pressure in stomach, increased after meals; loss of weight	Polyp in prepyloric segment		No	Gastrotomy and removal of polyp	Soft, gray, cherry-sized polyp on a long, thin stalk
8. Vanek, 1949	Female 56	Frequent spasms of pain in gastric region, radiating beneath left scapula, 3 months	Hypotonic stomach with ulcer above angulus		No	Gastric resection	Tumor the size of a small walnut, soft and yellowish, protruding above the level of the mucosa
9. Polayes and Krieger, 1950	Male 76	Intestinal obstruction and vomiting, 2 weeks	Neoplasm in middle third of jejunum	183	(?)	Resection of jejunum	Obstructing, 7 cm., fungating, annular mass in small bowel, with process extending through the wall to the serosa
10. Stout,* 1950						Gastric resection	Lesion discovered in stomach removed for ulcer
11. Booher and Grant, 1951	Female 59	Localized epigastric burning 1 hour after meals, relieved by lying down	Prepyloric polyp prolapsing into duodenum	106	No	Billroth I resection	Small sessile polyp 1.5 cm. in diameter

*Reported by Polayes and Krieger.

Physical examination revealed an obese woman whose blood pressure was 210/100 mm. of mercury. She had an aortic, systolic murmur. In the right side of the epigastrium there was point tenderness. No masses could be felt. The liver was not enlarged.

On May 2, 1950, a gastrointestinal series was done. The only significant findings appeared in the region of the pylorus, which filled and appeared normal. The duodenal bulb showed a constant filling defect approximately 1 cm. in size at the upper portion of its base (Fig. 1, *A*). This filling defect was constant, but could be made to move into the pylorus on manipulation (Fig. 1, *B*). The second and third portions of the duodenum appeared normal. Routine and spot films confirmed the diagosis of a 1 cm. polypoid tumor



A. *B.*

Fig. 1.—*A*, Radiograph showing a polypoid mass in the duodenal bulb. *B*, Manipulation reduces the prolapse of the polypoid lesion, the mass returning within the pyloric antrum.

with a long pedicle which appeared to arise in the pylorus, but which prolapsed into the duodenum. It could be moved back and forth through the pylorus by extrinsic pressure. The submitted x-ray films showed the same type of lesion.

The laboratory studies showed a hemoglobin of 15.4 Gm. and a white cell count of 5,300 with a normal differential distribution and a hematocrit of 47. The differential count showed 52 per cent filamented and 13 per cent nonfilamented polymorphonuclears, 2 per cent eosinophils, 15 per cent monocytes, and 28 per cent lymphocytes. The urinalysis was normal.

The patient was therefore gastroscoped, and, while the lower half of the stomach was adequately visualized and appeared to show a relatively smooth mucosa, no defect could be found in the pylorus or pyloric antrum.

The patient was admitted to the hospital and submitted to exploratory laparotomy on May 26, 1950. The only significant findings were in the pylorus and duodenum. On the lesser curvature side of the pyloric canal there was an indurated area in the wall which was surmounted by a 1.5 cm. polypoid mass which was quite freely movable. It could be made to prolapse through the pylorus into the duodenum with very slight pressure. The stomach was otherwise normal, as was the gall bladder. The remainder of the exploration was not significant. It seemed that we were dealing with an ordinary polypoid adenoma of the stomach for which a local resection with a subsequent Heineke-Mikulicz pyloroplasty would suffice, but which would be technically more difficult than the segmental resection. Accordingly, a Billroth I type of gastric resection was done.

The patient's postoperative course was uncomplicated, and she was discharged from the hospital on the fourteenth postoperative day.

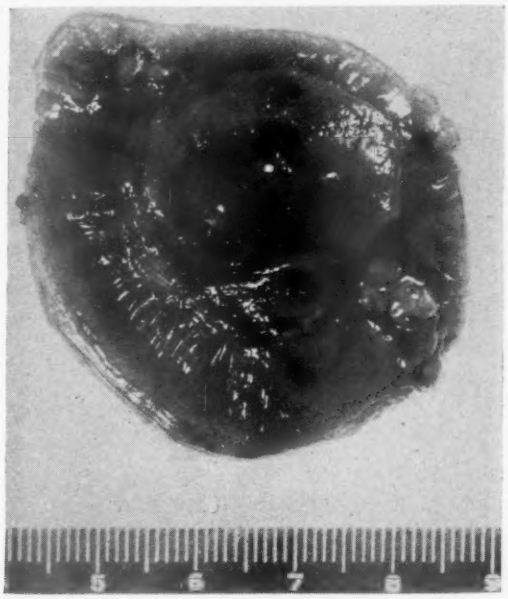


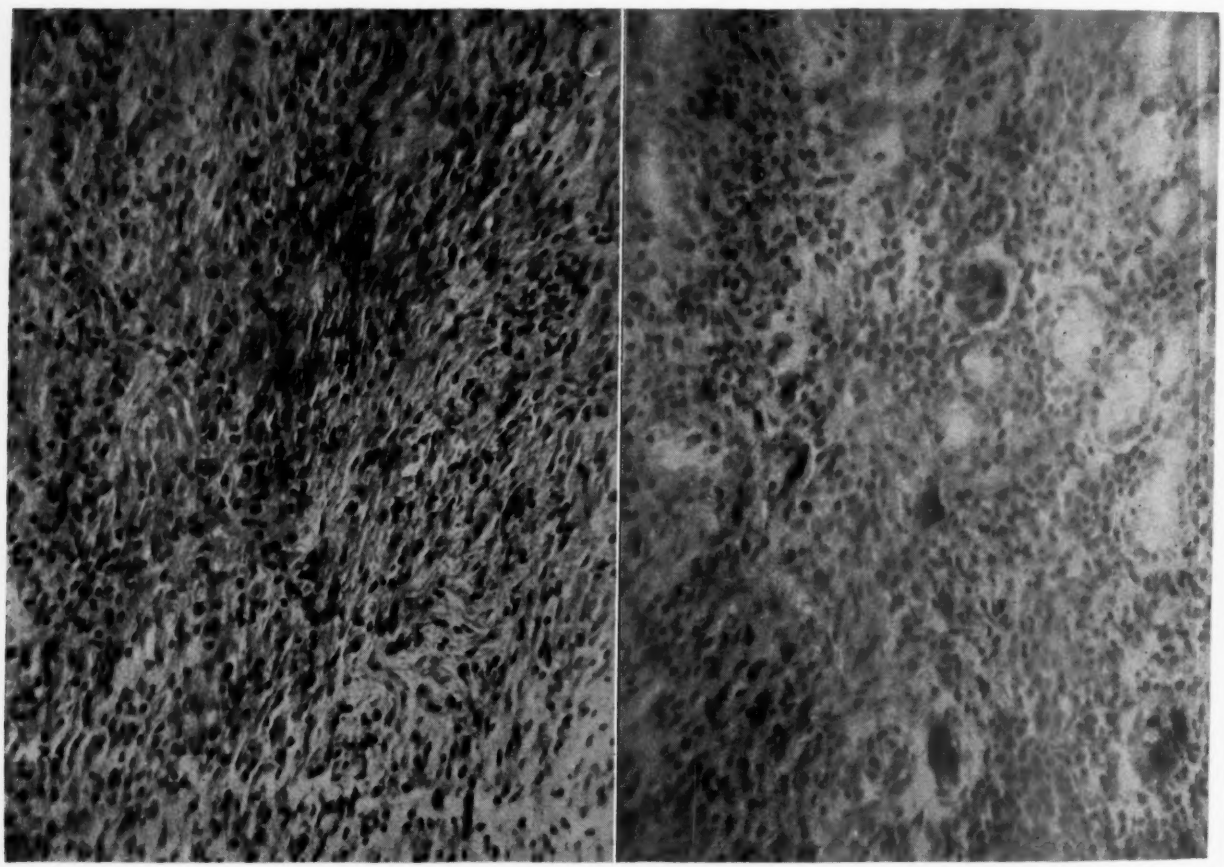
Fig. 2.—The resected eosinophilic granuloma, looking at the prolapsed polyp from the duodenal side of a Billroth I resection.

The report on the pathologic specimen (No. 50-7808) was as follows: The specimen was presented fresh and consisted of a segment of the pylorus measuring approximately 3 cm. in diameter and 6.5 cm. in length. There was a small sessile polyp measuring approximately 1.5 cm. in diameter and elevated approximately 0.7 cm. above the gastric mucosa. It seemed to rest 3 cm. from the proximal line of resection and 1 cm. from the duodenal line of resection. The mucosa over the polyp was smooth and entirely normal in appearance (Fig. 2). The histologic examination showed a marked infiltration of the submucosa with fibrocytes and eosinophils and a few histiocytes (Fig. 3, *A*). The reaction was most prominent in the submucosa but extended through the muscularis mucosae into the mucosa (Fig. 3, *B*). The diagnosis was Vanek's eosinophilic granuloma of the stomach.

Subsequent to the patient's discharge, she was questioned again regarding any allergic history. The only significant discovery was that early each summer for the past 5 years she had had a mild dermatitis over the hypothenar eminences bilaterally which disappeared after one or two days and which required no medication. In November an allergy study in the New York Hospital was entirely negative. The patient was without complaints when last seen on Dec. 20, 1950.

DISCUSSION

The most characteristic appearance of this process has been that of a prepyloric polypoid mass, which occurred in 8 of the 11 cases described. While all of them were not stalked polyps, the lesions were well circumscribed. The gross appearances of the lesions in all 6 of Vanek's cases are described as similar with some minor differences. The tumorlike tissue was situated mainly in the submucosa, forcing the mucous membrane up as a flat prominence in 2 instances, or in the form of a pendulous polyp, as it occurred in 3 cases. In one of his cases it was situated at the border of a calloused ulcer, as it was in



A. *B.*

Fig. 3.—*A*, Photomicrograph of the submucosal fibroblastic infiltrate showing numerous eosinophilic leucocytes and lymphocytes. *B*, Photomicrograph showing similar infiltration of the mucosa with eosinophilic leucocytes and lymphocytes.

Stout's case. On section, the tissue was grayish-yellow and soft, having an edematous appearance, while in the other cases it was white, firm, and elastic. In some cases the cut surface was studded with small openings which turned out to be dilated lymph spaces. Our patient presented a stalked polyp.

In the case reported by Barrie and Anderson the hypertrophy of the pyloric muscle was an associated process, but the granulomatous invasion was gen-

eralized. It apparently stands as an intermediary type of lesion to the remaining 2 cases in so far as the duodenum and first 2 feet of the jejunum also presented thickened, friable, indurated tissue similar to the generalized process in the pylorus. The report of Herrera and Guardia is quite similar, though in their case the entire small bowel was involved intermittently by bandlike induration similar to the diffuse process in the pylorus. Both of these cases presented a markedly edematous submucosa. The case of Polayes and Krieger was that of an exophytic, fungating granuloma confined to a segment of the jejunum.

The microscopic pathology has been summarized by Vanek. He stated the variations are quantitative ones between the amount of collagenous fibrils and the proportion of infiltrating cells. There are 3 essential components. The first component is composed of fusiform fibroblastic cells with a loose network of collagenous fibers through which irregularly distributed lymphocytes are found which occasionally accumulate to form rudimentary lymph follicles. The second component is formed by numerous eosinophilic polymorphonuclears which are distributed throughout the tissue, usually most marked in the deep submucosa and the muscularis, sometimes breaking the muscle fasicles into bands, with cavities appearing of various sizes from gross to microscopic proportions. These are filled with the third component, an eosinophilic, edematous material, "lakes of fluid" as described by Barrie and Anderson, and equally prominent in Herrera and Guardia's patient. In the latter's case, the presence of pararterial giant follicles was considered to represent a focus of early fibrinoid degeneration of an allergic type, quite similar to a type of reaction described in eosinophil myocarditis developing after neoarsphenamine treatment of syphilis.

The problem of etiology is disputed, and as noted by Barrie and Anderson, the possibility that such an organic change in the gastrointestinal tract could be produced by an allergic reaction is of great practical importance. Their patient presented a leucocytosis of 17,000 with an 18 per cent eosinophilia (3,060 per c. mm..), and 3 weeks later the eosinophilia was 31 per cent of an 11,800 count (3,685 per c. mm.). This persisted one month after surgery and they considered that the constant blood eosinophilia and the localized tissue eosinophilia of the pylorus represented an organic intestinal allergic reaction. It is most significant that this case, which presented gross extension of the process only second to that of Herrera and Guardia, and Herrera and Guardia's case are the only 2 cases presenting similar manifestations of eosinophilia. In the latter the admission white count of 16,800 showed no eosinophilia, whereas on the seventh postoperative day an 8,700 count was heralded by a 20 per cent eosinophilia (1,740 eosinophils per c. mm.), though no allergy of the patient is described. It is also most significant that in these 2 cases of extensive involvement, which also presented marked eosinophilia, a marked, and the greatest degree of, eosinophilic infiltration was described as occurring in the muscularis. In this respect, it is pertinent to allude to Barrie and Anderson's interpretation of the phenomena in stating that Kaijser[6] pointed out that in one of his cases, cited to illustrate the importance of the recognition of allergic

factors by the surgeon, the eosinophilic infiltration mainly in the muscle of the small bowel might indicate that the antigen was a parenteral one, whereas when the infiltration was mucosal and submucosal, the antigen presumably was a peroral one. This, however, seems to be a conjecture and cited in their case because the pararterial giant follicles in the pylorus closely resembled follicles found in the heart muscle of patients who had become sensitive to neoarsphenamine. Barrie and Anderson's patient presented a negative Wassermann reaction, but Herrera and Guardia's case presented a positive Kahn, apparently without treatment. Whether or not the eosinophilia represented an isolated allergic reaction or a response to penicillin therapy is doubtful, and Coppinger and Goldner's[7] observation that penicillin therapy may elevate the eosinophil count makes this isolated fact a very difficult one to assess. As far as eosinophilia is concerned, Page[8] and others have shown that eosinophilia itself is of no diagnostic value in gastrointestinal complaints except in intestinal parasitic diseases.

Because of the postoperative eosinophilia in these 2 cases, at least casual mention must be made of the third case of Kayser's. This patient was a 53-year-old man with a marked allergic history who, 9 days after gastrectomy for ulcer, presented a blood eosinophilia of 26 per cent and a gastric mucosal and submucosal eosinophilia occurring in the similar setting of marked gross submucosal edema, though this case was not reported as this type of granuloma.

In the localized or nodular processes, allergy has not appeared to be a factor. No allergy could be determined by skin testing in our patient. Vanek reviewed the clinical histories of his patients and could find nothing definite in this respect, nor did the hemograms indicate anything in particular, since all hemograms were, at most, only approaching the upper limit of normal. In the case of solitary involvement of the jejunum, there was no significant eosinophilia (3 per cent of 6,100 leucocyte count—183 per c. mm.) nor was there an allergic history, though there was a positive skin test with oidium and tricophyton allergens.

While the etiology cannot be stated, the marked similarity of the 2 cases with greatest extent of granulomatous involvement, both with blood eosinophilia and similar tissue distribution of eosinophilic infiltration, would seem to present the strongest argument in favor of renewed interest in the allergic background of this disease, especially since it has attended those cases of greatest gross change.

Allergy did not appear to be a factor in the localized or nodular processes in Vanek's cases nor in ours, though Vanek stated that the outstanding eosinophilic infiltration is suggestive of some allergic phenomenon.

Herrera and Guardia concluded that the lesion is an inflammatory one of subacute or chronic nature producing a pseudophlegmonous thickening of the pyloric walls and subsequent stenosis. Vanek considered the lesion as a granuloma, though he admitted that in some cases in which the infiltration of migratory cells has receded the lesion may be difficult to differentiate from a fibroma. Since no etiological facts can be discovered, the true nature of the process can-

not be identified. However, recognition of a process is in order, which, as expressed by Vanek, is composed of pathologic tissue appearing predominantly as a circumscribed focus in the submucosa of the stomach, causing a bulging and in a majority of the cases a polypous formation. While the process is predominantly one of the pyloric antrum, it may extend into the small bowel and here may even have multiple sites of origin. The rather diffusely involved areas, however, strongly indicate the lesion to be an inflammatory one of chronic granulomatous character, rather than a fibroma with secondary inflammatory reaction.

SUMMARY

1. The problem of eosinophilic granuloma of the upper gastrointestinal tract is reviewed.

2. Eleven cases are collected, 8 occurring as solitary processes in the stomach, 1 in the jejunum, and 2 involving the distal stomach, duodenum, and small intestine.

3. Those cases presenting greatest gross pathologic change have been attended by a blood eosinophilia which, when considered with the local gastrointestinal tissue eosinophilia, may indicate an allergenic background which, however, is not apparent in the solitary form.

4. A case of solitary prolapsing submucosal eosinophilic granuloma is presented.

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Surgical Technique

THE RIGHT THORACOABDOMINAL APPROACH TO LESIONS OF THE COMMON BILE DUCT

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IT IS axiomatic that the secret of good surgery lies in adequate exposure and nowhere is exposure more important than in dealing with lesions of the common bile duct. In a recent classic article, Lahey and Pyrtek[1] have re-emphasized the dangers and difficulties involved in the repair of common duct strictures. These patients have usually been subjected to many previous laparotomies and dense adhesions obscure the biliary tract. It is often necessary to mobilize the common duct up to the liver hilus and this may be difficult because of the overhanging liver and the unyielding costal margin.

Heaney and Humphreys[2] have recently outlined the anatomic details of the right thoracoabdominal incision and pointed out its potential value in lesions of the common bile duct. Several authors[3, 4] have reported the satisfactory use of this approach for portacaval anastomosis.

Two years ago we decided to utilize this incision for strictures of the common bile duct. As experience accumulated, we became so impressed with the superb exposure afforded and the relative lack of morbidity in the postoperative period that we adopted the incision for all recurrent operations on the bile ducts. We have now used the right thoracoabdominal approach in sixteen operations on the common bile duct and we feel that it represents a real advance in the surgery of this difficult region.

OPERATIVE TECHNIQUE

The patient is placed in position on the operating table with a small sandbag under the right scapula and another under the right buttock. The table break is beneath the lower ribs and the foot and head are lowered to put the operative site on the stretch (Fig. 1).

An incision is made along the eighth rib from the mid-axillary line to the mid-line of the abdomen. The eighth rib is resected and the costal arch divided. The abdominal portion of the incision is carried down to the peritoneum, incising the rectus sheath and dividing the right rectus muscle. The pleural and peritoneal cavities are opened and the wound is spread with a Burford retractor. The diaphragm is divided from the costal margin toward the vena cava and the liver is displaced upward into the chest. The transverse colon is freed from the liver and retracted downward, exposing the duodenum, which is mobilized as recommended by Lahey and Pyrtek.[1] This maneuver exposes the common bile duct throughout its entire length. The table is rotated to the

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left and the structures of the hepatic pedicle are approached from the lateral aspect, avoiding the adhesions which are usually most dense anteriorly. The duct then lies superficially and wide exposure facilitates dissection and suturing. Fig. 2 illustrates the exposure afforded by this method of approach.

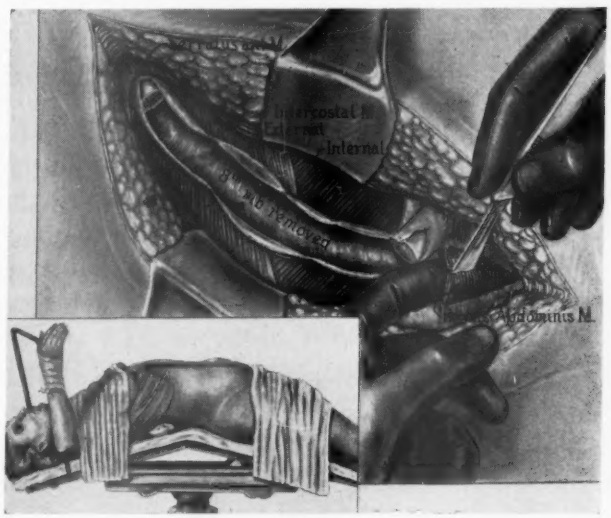

Fig. 1.—The right thoracoabdominal incision. Inset shows the position of the patient on the operating table.

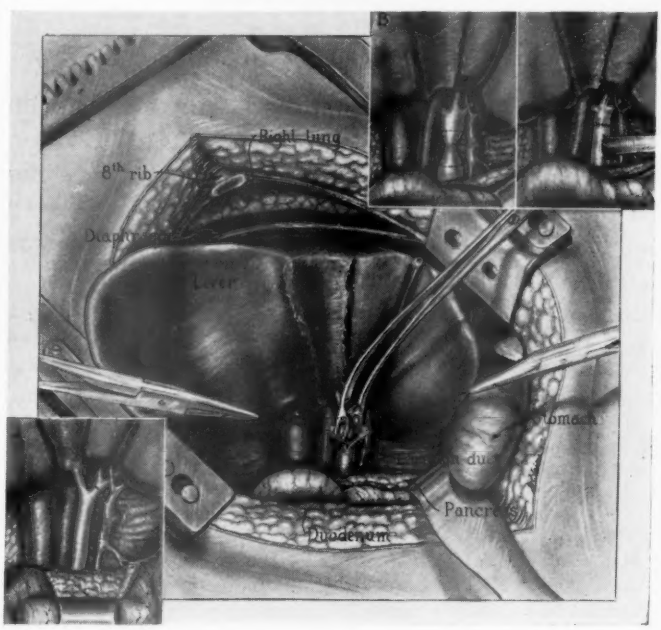

Fig. 2.—Exposure of biliary ducts afforded by the thoracoabdominal approach.

The common bile duct has been explored in sixteen cases through an abdominothoracic incision. In eight cases a traumatic stricture was found which was repaired by the Heineke-Mikulicz method in two and by excision with end-to-end suture over a T tube in six. In four cases, residual stones were found in

the duct. In two instances a stricture at the sphincter of Oddi was discovered and treated by transduodenal division with insertion of a long-limbed T tube. In one case the duct was angulated by adhesions but no intrinsic pathology was present and in one exploration was completely negative. In all cases, adequate exposure was obtained with relative ease. It has been the unanimous opinion of surgeons at this hospital that the displacement of the liver into the chest, the elimination of the costal overhang, and the approach to the duct from the posterolateral aspect offer an exposure which is difficult or impossible to obtain through the conventional abdominal incision.

The wound is closed by joining the cut edges of the diaphragm with interrupted sutures, approximating the cut costal margin, and suturing the abdominal and thoracic incisions in the usual fashion. A catheter is placed in the chest wound and withdrawn as the lung is expanded at the close of the operation. The T tube is brought out through the medial end of the abdominal incision.

The criticism has been offered that opening the chest might cause a higher mortality and morbidity. There have been no deaths in this series and four patients have had minor complications due to the chest incision, three developing pleural effusion and one intercostal neuralgia. In the remainder the postoperative course has been uneventful and the average time of hospitalization the same as in abdominal cases. We do not feel that the slight increase in morbidity outweighs the advantages of this approach.

SUMMARY

1. The right thoracoabdominal approach to the common bile duct is described.

2. This incision has been used in sixteen cases and has given an unparalleled exposure of the region.

3. There has been no mortality in this series and the increase in morbidity due to the thoracic incision has been of little importance.

4. The right thoracoabdominal incision is recommended in cases with previous biliary tract surgery.

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Editorial

Neoplasms—Expanding, Infiltrating, Metastasizing

Neoplasia is the new formation of atypical tissue. The problem of neoplasia involves the process of cell division, the factors determining the evolution of cells, the formation of tissues and their grouping into organs—in short, the basic principles of growth itself. Although the finer details of these phenomena are not fully understood, a great body of knowledge is available for practical use. The microscopic structure and the behavior of most human neoplasms have been fairly adequately explored. Since the structure of a neoplasm provides clues as to its behavior, it is now generally accepted that the structure of a neoplasm should be determined before treatment is instituted.

According to present knowledge, neoplasms are derived from cells of the individual. The neoplastic cells making up a growth are either of anlage origin or of body cell origin. Those of anlage origin arise from hitherto dormant cells left over in the process of evolution of the individual. Those of body cell origin arise from cells of the individual still capable of cell division. When a neoplastic cell arises, be it of anlage or of body cell origin, this cell has certain tendencies of its ancestor cell. These tendencies reveal themselves when the neoplastic cell multiplies and attempts to reproduce the patterns usually formed by its ancestor cells. There are, however, neoplasms so undifferentiated that their cellular origin remains undetermined. In such instances the cells multiply and produce bizarre structures without revealing any clues as to their cellular origin. Most neoplasms, however, present a sample mimicking some part of the germ layers or a sample of some tissue in a phase of its development from embryonic to fetal or adult stage.

Neoplasms may grow expansively like a toy balloon, pushing and compressing rather than invading the surrounding tissues. These expanding neoplasms are to be distinguished from those growing infiltratively, extending with fingerlike processes into surrounding tissues, invading and replacing them. The cells of these infiltrating neoplasms may or may not become transported and transplanted into regional lymph nodes or distant organs. The neoplasms whose cells become detached and are carried by the lymph or by the blood stream to distant parts where they set up foci similar to the cancer at the site of origin are metastasizing neoplasms. These terms, expanding neoplasms, infiltrating neoplasms, and metastasizing neoplasms, express more exactly the behavior of the neoplasm than do the terms benign and malignant, and therefore are preferable.

Whether a neoplasm is expanding, infiltrating, or infiltrating and metastasizing is of immediate concern to those dealing with patients who have a neoplastic disease. The handling of an expanding neoplasm is uncomplicated.

Complete surgical removal will cure it. Infiltrating neoplasms, like expanding neoplasms, are curable by surgical removal, particularly in their incipient stages when they are still in situ, that is, in or near the location where they originated. Infiltrating neoplasms may be destroyed by irradiation. If treated by either method, cure may be obtained only if all of the cancer cells are completely removed or killed. When the neoplasm is treated by irradiation, an adequate—killing—dose has to be delivered over the entire area of involvement within an orbit of uninvolved tissue. When treated surgically, the operator must keep outside the cancer field and remove the involved area within a zone of uninvolved tissue. Entering the cancer field and touring it, or removing it by "controlled excision" with frozen section is of questionable value to the patient. Transplantation of cancer cells experimentally or inadvertently has proved again and again that the rule of not entering the cancer field cannot be violated without dire consequences to the patient.

Infiltrating neoplasms after they have metastasized to regional lymph nodes can be cured only if the entire area of involvement is removed. In case of a carcinoma, for example, the site of involvement, the regional lymph nodes, and the path between the two must be removed in contiguity. The entire area of involvement often cannot be removed. Following operation, irradiation of the area that may still contain cancer cells aims at the destruction of residual cancer cells.

At present, infiltrating neoplasms which have metastasized widely and to distant organs are not curable by any surgical procedure nor can they be cured by direct methods of irradiation. The hope for improved treatment probably lies in chemotherapy combined with isotopes. This is an active field of research with as yet few tangible results.

Béla Halpert.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE PRESENT STATUS OF TOTAL GASTRECTOMY IN THE TREATMENT OF GASTRIC CANCER

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IN SPITE of the extensive research efforts of recent years, the grim fact remains that the only hope for the patient with cancer of the stomach lies in complete surgical extirpation of the lesion. And at best it is rather a slender hope. Recent reviews of the subject[50, 64, 75] indicate that, of 100 patients with gastric cancer presenting themselves for treatment, probably not more than 80 will be operated upon, about 50 will have resectable lesions, and less than 10 will survive for 10 years after operation.

Earlier diagnosis is an obvious and necessary approach to the problem. Large-scale screening of the population by various methods now under study[60, 64] will doubtless pick up some early, unsuspected cases of gastric cancer, but, in spite of everything, the majority of patients suffering from this insidious disease will continue to come to the surgeon with well-advanced lesions. Until a more fundamental solution of the cancer problem is found, it is obvious that our surgical horizons must be broadened in an effort to save a larger number of these patients. Several surgeons[38, 45, 63] have suggested that a partial solution may lie in the adoption of total gastrectomy in place of partial gastrectomy as the standard radical operation in the treatment of all resectable gastric cancers. Such a viewpoint has been emphasized recently in editorials by Lockwood[37] and by Lahey.[32]

Before we adopt such a radical policy we must answer several fundamental questions.[32] Can total gastrectomy be performed with a mortality rate comparable to that of partial gastrectomy, and, if so, what factors are important in attaining such results? Can patients surviving after total gastrectomy maintain a reasonable state of nutrition, general health, and comfort over a period of years? Is there a reasonable hope of increasing the curability rate by the application of the principles of total gastrectomy in all cases of gastric cancer?

It is in an effort to answer these questions from the combined experience of many investigators that this survey is presented. Excellent collective reviews of the literature on the subject of total gastrectomy have been published by Finney and Rienhoff in 1929,[15] by Roeder in 1933,[59] and by Pack and

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McNeer in 1943.[47] These reviews, supplemented by a representative selection from the papers which have appeared in the English literature within the last ten years, form the basis of the present summary.

HISTORICAL REVIEW

Total gastrectomy was first performed by Phineas Conner of Cincinnati in 1884, only 3 years after Billroth introduced the procedure of partial gastrectomy for the treatment of cancer, but Conner's patient died on the operating table. The operation was successfully accomplished in 1897 by Schlatter of Switzerland, whose 56-year-old patient survived 1 year and 53 days after total resection of the stomach and esophagojejunostomy. The following year 2 American surgeons, Brigham and Richardson, each reported a successful total gastrectomy, as did Harvie in 1900, Moyihan in 1903, and W. J. Mayo in 1917.

In 1929 Finney and Rienhoff[15] collected from the literature 67 cases of total gastrectomy with a mortality of 53.8 per cent and added 5 personal cases. Four years later Roeder[59] reviewed 88 cases with a mortality of 50 per cent. An increasing application of the technique of total gastrectomy to the problem of gastric cancer was evidenced by the fact that in 1933 Pack and McNeer[47] were able to collect reports of 303 cases. The operative mortality had fallen to 36.9 per cent, but still remained disturbingly high.

Within the last 10 years many surgeons have interested themselves in the problem of total gastrectomy. Technical advances, together with recent advances in anesthesia, chemotherapy, and general surgical care, have enabled a number of clinics to report mortality rates in the neighborhood of 10 per cent in recent series of operations.[32, 61, 71, 73] The indications for the operation have been correspondingly widened until some envisage the future use of total gastrectomy as the procedure of choice in the treatment of all forms of gastric carcinoma.[32, 37, 38, 45, 63]

INDICATIONS FOR TOTAL GASTRECTOMY

In discussing the indications for total gastrectomy, Graham[22] has remarked: "The enthusiasm which the individual surgeon displays for this operative procedure will depend largely on his philosophy of life. If such philosophy demands that all efforts be used to prolong life, even though the effort be accompanied by grave immediate risk, and though the patient ultimately must die from carcinoma, providing he lives long enough, then such a surgeon must be an advocate of total gastrectomy."

It is true that the procedure of total gastrectomy is technically difficult and has been accompanied in the past by high operative mortality rate and a low rate of curability when applied to malignant lesions. On the other hand, this survey will emphasize that the mortality rate has been sharply reduced during the last 10 years and that, though there are relatively few "cures," many patients reported in recent series have lived for several years with marked relief of symptoms after total gastrectomy for advanced carcinoma.

Brunschwig,[5] Lockwood,[37] and others have emphasized that future progress in cancer surgery must lie in the direction of a bolder operative approach and an extension of the indications of operability. Certainly this is true of the application of total gastrectomy to the problems of carcinoma of the stomach.

In a recent discussion of the principle governing total gastrectomy, Pack, McNeer, and Booher[48] have suggested the following indications for the operation: (1) carcinoma of such a size and in such a location that it cannot be completely removed by subtotal resection of either the distal or the proximal portion of the stomach; (2) carcinoma of the diffuse or linitis plastica type; (3) lymphosarcoma; (4) malignant leiomyoma or leiomyosarcoma; and (5) multiple, diffuse polyposis *en nappe* or polypous gastritis. This is essentially the position of the Mayo Clinic group,[71] who stated, "When it is possible to remove tissue well beyond the lesion by partial gastrectomy, when microscopic examination at the time of operation shows that at least 2 inches (5.1 cm.) of tissue has been removed beyond the uppermost limit of the lesion, and when there is a cuff of duodenum beyond the point of possible extension of the malignant lesion, partial gastrectomy is preferable to total gastrectomy."

To be amenable to treatment by total gastrectomy the lesion must, of course, be confined to the limits of the stomach and the regional lymph nodes. It does not seem justifiable at the present time to employ total gastrectomy as a palliative procedure in the presence of grossly evident distant metastases. Livingston and Pack[36] have emphasized, however, that over 20 per cent of individuals who die of gastric carcinoma are free of any evidence of distant metastases at autopsy. It is essential, therefore, that every patient upon whom the diagnosis of carcinoma of the stomach is made should be carefully explored and evaluated from the standpoint of possible extirpation of the lesion by subtotal or total gastrectomy.

A number of surgeons have begun to explore the possibility of extending the indications for total gastrectomy to include all malignant neoplasms of the stomach. Longmire and Scott[38, 61] argue that such an operation is more in keeping with generally accepted principles of cancer surgery and that the mortality of total gastrectomy need not be excessive if the operation is applied to less advanced lesions. They present a series of 63 cases with 6 operative deaths, a mortality of 9.5 per cent. Morton[45] has also performed total gastrectomy for 2 cases of only moderately advanced carcinoma, and Smithwick[63] has considered the adoption of such a policy.

This approach is supported by the observations of Verbrugghen[69] on the intramural spread of gastric carcinoma. A study of 50 resected specimens revealed the presence of tumor cells as much as 4 cm. beyond the palpable or visible edge of the tumor in many cases. In 9 cases the line of resection was not clear of the tumor. Coller, Kay, and McIntyre,[12] in an excellent study on the intramural and extramural lymphatic spread of gastric carcinoma, observed that metastases to regional lymph nodes were present in 75.5 per cent of cases, and that in 23.5 per cent there was microscopic extension of the tumor to the line of resection when high subtotal gastrectomy was done. They em-

phasized the importance of resection wide of the tumor and the completest possible removal of all 4 zones of regional lymphatic metastases corresponding to the vascular supply of the stomach (Fig. 1). Lahey[32] pointed out that this ideal in the surgery of gastric cancer can be attained only by the total resection of the stomach, together with the spleen, the entire greater omentum, and the lymph nodes in the region of the cardia and the pylorus. He urged that such resection should be undertaken by qualified surgeons in the treatment of all cases of gastric cancer, early or advanced, so that their combined experience may form a basis for eventual decision as to the merit of the method.

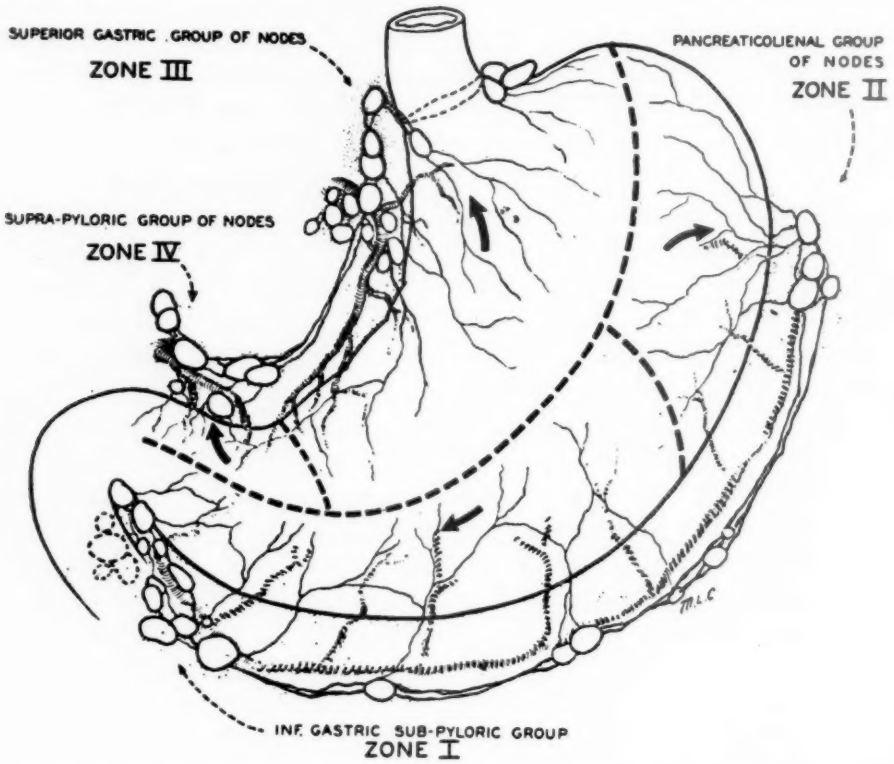

Fig. 1.—Zonal lymphatic metastases of carcinoma of the stomach. (From Coller, Kay, and McIntyre.[12])

With the development within the last 10 years of the operation of transthoracic partial gastrectomy, partial esophagectomy, and esophagogastrectomy for the treatment of carcinoma of the cardia of the stomach and the lower esophagus, an alternative to total gastrectomy in the management of these lesions is now available. The operation was introduced in this country by Adams and Phemister,[1] developed by Garlock,[17] Churchill and Sweet,[8, 9] and Phemister,[52] and is now a well-established procedure in many clinics.[4, 20, 49, 51, 67] The mortality rate in a series of 227 resections of this type, collected from 4 recent reports,[4, 49, 51, 67] was 20.7 per cent, or approximately the same as that which prevails for total gastrectomy. However, when cardiectomy is con-

sidered, the facts just quoted in regard to the intramural and lymphatic spread of gastric carcinoma must be borne in mind, and the operation should be applied only to lesions which are strictly localized to the lower esophagus or cardia. More extensive lesions of the proximal portion of the stomach should be treated by total gastrectomy, which is no more difficult technically, involves a comparable mortality rate, and represents a more adequate operation for cancer. Of 122 patients with cancer involving the gastric cardia, Pack and McNeer[49] found that 62 could be treated by cardiectomy, while 60 were subjected to total gastrectomy.

PREOPERATIVE PREPARATION

The importance of careful preparation of, or operation upon, the elderly, debilitated patient with gastric carcinoma has been emphasized by Ravdin and associates,[55] Wangensteen,[72] and others.[8, 49] A week to 10 days of active treatment is required in the average case for the correction of the pathologic physiology of gastric obstruction and dilatation, dehydration, electrolyte depletion, anemia, diminished blood volume, hypoproteinemia, and avitaminosis.

The local condition of the obstructed stomach is improved by continuous gastric suction combined with frequent lavage with 0.1 N hydrochloric acid to inhibit bacterial growth. Dehydration and electrolyte depletion are corrected by the intravenous administration of solutions of glucose, sodium chloride, potassium chloride, and other electrolytes as indicated. Frequent transfusions of whole blood are given to restore the hemoglobin concentration and the blood volume to normal.[10, 11] In the absence of pyloric obstruction the correction of hypoproteinemia and avitaminosis is best carried out by the oral intake of a high protein, high vitamin diet, with a total caloric value of 4,000 to 5,000 calories, divided into frequent feedings. For those with some degree of pyloric stenosis Wangensteen[72] recommended the continuous intragastric drip feeding of a liquid diet containing 408 Gm. of protein, 114 Gm. of carbohydrate, and 37 Gm. of fat per liter. Three liters of the feeding contain 4,800 calories. Vitamin C, the vitamin B complex, and vitamin K are added as required. If complete obstruction at the pylorus or at the cardia precludes any nutritional intake by mouth, the patient must be prepared for operation by the parenteral administration of protein hydrolysates, carbohydrate, electrolytes, and vitamins in adequate quantities. In an excellent review of the extensive literature on the subject, combined with a report of some original metabolic studies, Kremen[28] concluded that the most satisfactory preparation of patients of this type is achieved by the daily intravenous administration of 500 c.c. of whole blood and 3,000 c.c. of 5 per cent protein hydrolysate in 5 per cent glucose solution, provided the cardiovascular system of the patient will tolerate such quantities of intravenous fluid. On this regime a positive nitrogen balance was consistently established and a representative group of poor-risk patients showed an excellent tolerance to major surgical procedures after a week of preparation. Vitamin C, vitamin B complex, and vitamin K should be added daily to the intravenous solution.

Anemia, diminished blood volume, hypoproteinemia, and avitaminosis undoubtedly contributed greatly to the previous high mortality of total gastrectomy and particularly to the high incidence of sepsis due to leakage at the anastomosis. It has been demonstrated beyond question that healing is greatly retarded in the presence of hypoproteinemia or a deficiency of essential vitamins.[34, 68, 76] The effect of proper appreciation of these factors is seen in the decreasing mortality rates reported in recent series of cases.

ANESTHESIA

The choice of anesthesia depends upon the procedure contemplated by the surgeon. If the thorax is opened, intratracheal positive pressure anesthesia, using ether or cyclopropane and oxygen, is required. For transabdominal procedures continuous spinal anesthesia by the method of Lemmon[35] is considered by many the method of choice, because of the excellent relaxation obtained and the good condition of the patient throughout a prolonged procedure.[33, 48] Alternatively, intratracheal inhalation anesthesia combined with curare may be used, particularly if there is a possibility of extending the incision into the chest. Needless to say, the choice of the anesthetic agent is not nearly as important as the presence in the surgical team of a skilled and responsible medical anesthetist, who will control the anesthesia and adjuvant supportive therapy to meet the varying requirements of the patient during the course of the operation.

CHOICE OF SURGICAL APPROACH

Total gastrectomy may be accomplished by the transabdominal approach, by a transthoracic, transdiaphragmatic approach, or by the combined abdominothoracic approach.

The great majority of total gastrectomies have been done transabdominally, using a vertical or transverse upper abdominal incision. Adequate exposure of the abdominal esophagus is obtained in most cases after division of the triangular ligament, retraction of the left lobe of the liver toward the right, and division of the vagus nerves. With few exceptions, the operations summarized in Table II were accomplished transabdominally. This approach probably remains the method of choice in cases in which the lesion does not involve the cardia or esophagus, in which the esophagus can be mobilized sufficiently for the comfortable completion of a subdiaphragmatic anastomosis, and in which satisfactory exposure is not prevented by obesity or the contour of the thorax.[31, 39]

The development in recent years of the transthoracic, transdiaphragmatic approach for the resection of lesions of the lower esophagus and cardia of the stomach has been discussed previously. This technique was first applied to total gastrectomy by Meyer,[42] in 1942, and subsequently by Sweet.[65, 66] It affords excellent exposure for dealing with lesions which have involved the cardia of the stomach and lower esophagus and for performing an esophagojejunostomy above the diaphragm. The removal of the lymph nodes along

the left gastric and left gastro-epiploic arteries is readily accomplished, but exposure may be a limiting factor in resection of the greater omentum, dissection of the supra- and infrapyloric nodes, and closure of the duodenal stump. There is the additional disadvantage that the thoracotomy and incision of the diaphragm must be performed before one has an opportunity to judge the operability of the lesion. In a series of 32 patients operated upon by this technique at the Massachusetts General Hospital from 1942 to 1946, Welch and Allen[75] reported an operative mortality of 28 per cent, a figure somewhat higher than the average for recent series of transabdominal operations as noted in Table II.

Garlock[18] and Humphreys[24] recently suggested a combined abdominothoracic approach to the stomach, utilizing an upper abdominal incision extended into the thorax through the eighth interspace and dividing the diaphragm down to the esophageal hiatus. A similar approach, using a transverse upper abdominal incision extended into the thorax, was previously described by Kirschner[27] and has been adapted for total gastrectomy by Kremen.[29] The incision affords ideal exposure for both the abdominal and the thoracic parts of the procedure and the gastric lesion may be explored for operability before a thoracic or diaphragmatic incision is made. The lower part of the esophagus is readily resected if required and a tension-free esophagojejunostomy may be performed either above or below the diaphragm, according to the extent of the esophageal resection.

The only contraindication to the abdominothoracic approach is the increased magnitude of the operative procedure and the possible increase in operative shock and in postoperative pulmonary and cardiac complications. Garlock[19, 20] and others[6, 29, 57] felt that the opposite is true, due to better exposure, gentler dissection, and more accurate anastomosis under these conditions. Kremen[29] reported on the use of the abdominothoracic incision for total gastrectomy in a series of 6 patients. One patient died 8 days after a very extensive resection of a lesion involving the pancreas, transverse colon, and jejunum—a mortality rate of 16.6 per cent. To the best of our knowledge no large series of total gastrectomies using the abdominothoracic incision has been reported. We consider that the combined approach for total gastrectomy is indicated when carcinoma involves the cardia or esophagus and when exposure by the transabdominal route proves unsatisfactory. If the indications for total gastrectomy are broadened to include all gastric cancers, many of the smaller tumors will be managed transabdominally without difficulty. However, the surgeon should not hesitate to extend the incision into the chest should the need arise.

TECHNIQUE OF TOTAL GASTRECTOMY

Abdominal Exploration and Determination of Resectability.—This is the first step in either a transthoracic or a transabdominal procedure. The abdomen is first examined for evidence of distant metastases to the liver, pelvis, root of the mesentery, and visceral or parietal peritoneum. The location and extent of the gastric lesion and the mobility of the stomach are explored. The

gastrocolic and gastrohepatic omenta and the transverse mesocolon are carefully inspected for evidence of extension of the lesion. The esophagus and cardia are palpated to determine whether the presence of tumor in this area will necessitate an abdominothoracic procedure.

If the lesion, however advanced or bulky it may be, is limited to the stomach and the regional lymph nodes, resection should be carried out. Even direct extension to involve the transverse colon, pancreas, or spleen does not necessarily preclude resection, since these structures may be resected en bloc in suitable cases.

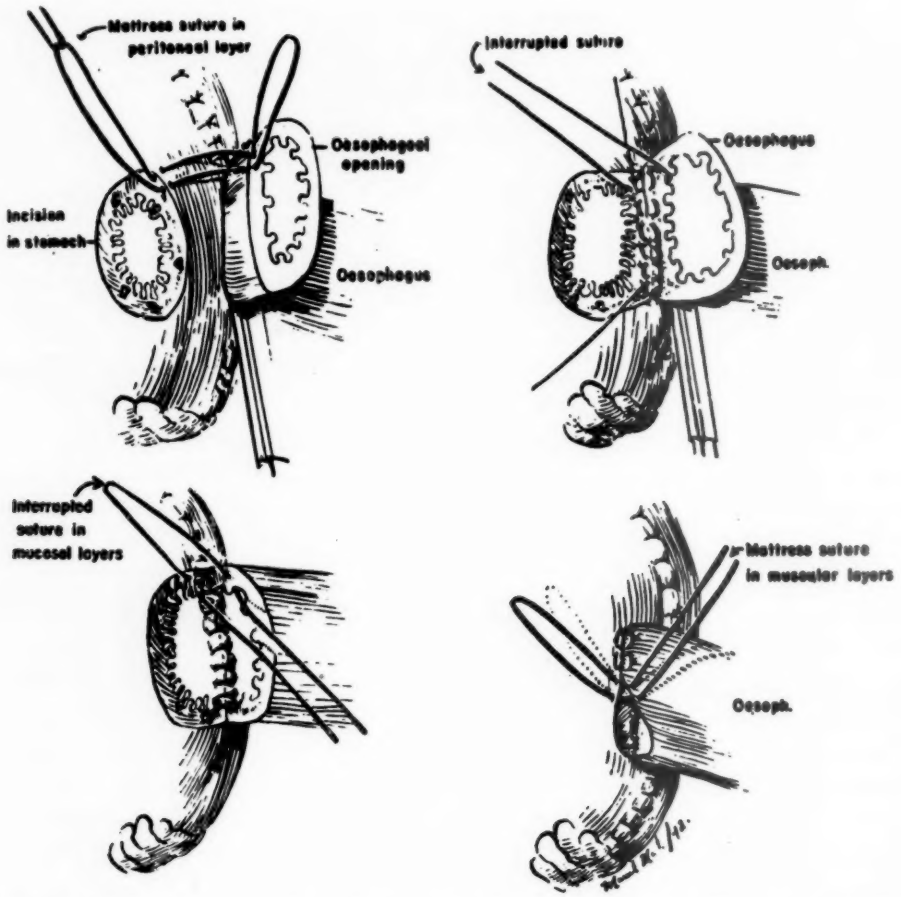

Fig. 2.—Technique of esophagogastrostomy. The method is equally applicable to esophagojejunostomy. Interrupted sutures of fine silk are used throughout. (From Churchill and Sweet.[4])

Scope of the Resection.—The operation of total gastrectomy for cancer should be planned and executed in keeping with the well-established principles for the radical extirpation of cancer elsewhere in the body. The procedure should envisage the resection en bloc of (1) the entire stomach, including the pylorus and the cardia and, if necessary, the lower esophagus; (2) the perigastric tissues, including all the lymph nodes of the subpyloric, pancreaticolienal, superior gastric, and suprapyloric groups (Fig. 1)[12]; (3) the

entire greater omentum. An excellent description of the technique of performing this excision is provided by Lahey[31] (Fig. 3, *A-F*). Surgeons differ in their opinion as to the advisability of removing the spleen with the stomach. Lahey advised routine splenectomy, with the argument that it simplifies the technical procedure, extends the scope of excision of lymphatics in this area, and does not add to the mortality. Graham[22, 23] avoided the removal of the spleen because of the possible occurrence of postoperative thrombosis due to the increased platelet count following splenectomy. In this connection Quan and Castleman[53] studied a group of 70 patients who had splenectomy incidental to gastrectomy or esophagectomy. Eighteen patients died postoperatively

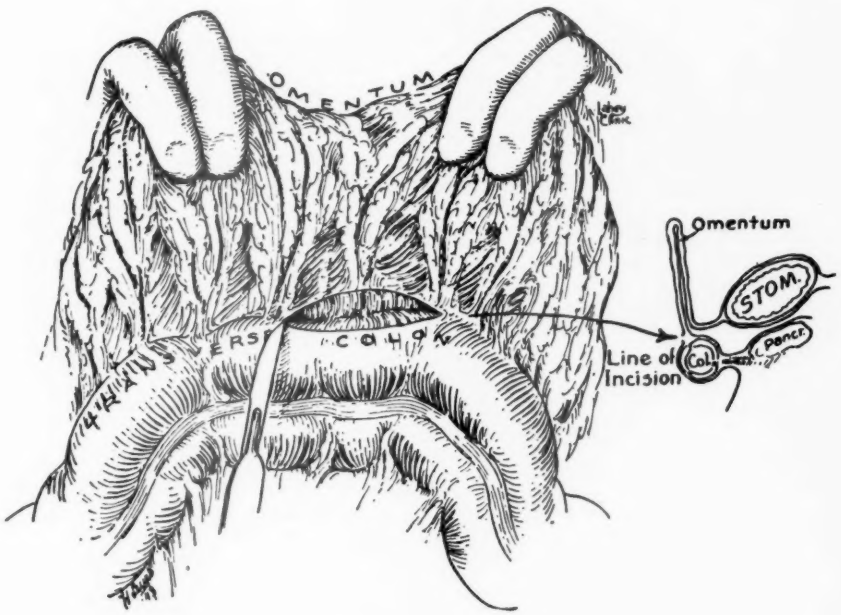

Fig. 3, *A*.—Technique of total gastrectomy.
The first step in the separation is sharp dissection of the omentum from the transverse colon. Note the avascular line of cleavage. Note the developmental line of cleavage and the line of incision in the avascular area (insert). (From Lahey and Marshall.[33])

and 17 were studied at post-mortem examination. Five showed extensive thrombosis of the splenic and portal veins and in one instance this thrombosis, extending to the superior mesenteric vein, was the direct cause of death. Of the 52 survivors only one had a clinical course suggesting splenic vein thrombosis. Most surgeons are agreed that one should not hesitate to include the spleen in the excision if there is any evidence of involvement of the nodes of the splenic pedicle or if the operative procedure is facilitated thereby. The transverse colon or tail of the pancreas may be involved by direct extension of the tumor. These structures may be resected en bloc with the stomach if there is no evidence of distant metastases and provided the condition of the patient warrants such an extensive procedure. Operations of this type have been carried out by Brunschwig[5] and others with some encouraging results.

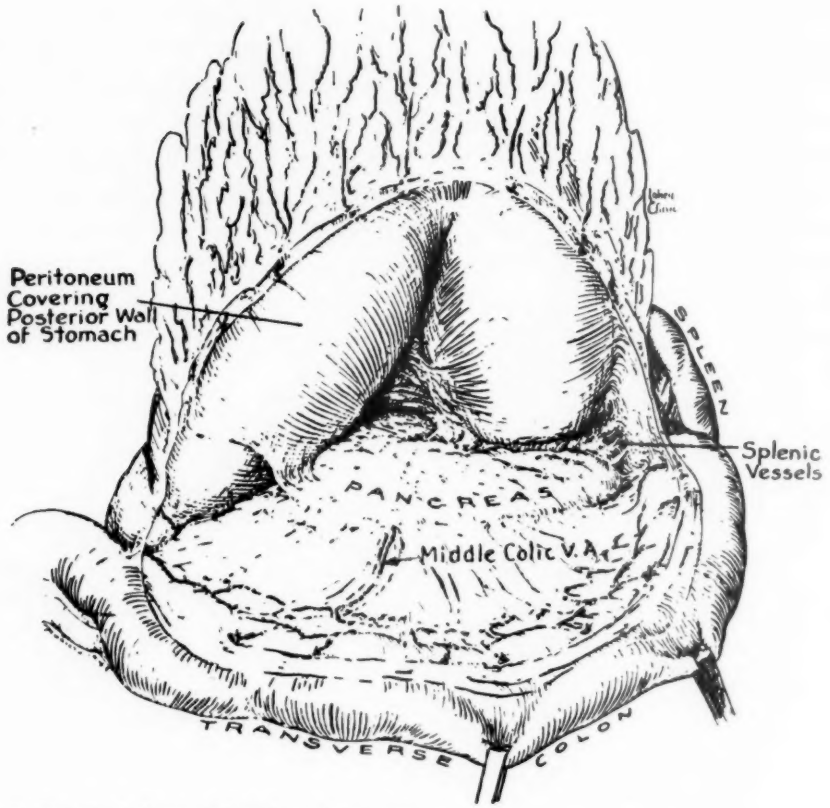

Fig. 3, *B*.—Technique of total gastrectomy.

The omentum is completely separated from the transverse colon and is still attached to the greater curvature. The pancreas is visualized, and the stomach is turned up. Note the splenic vessels beyond the tip of the pancreas. (From Lahey and Marshall.[33])

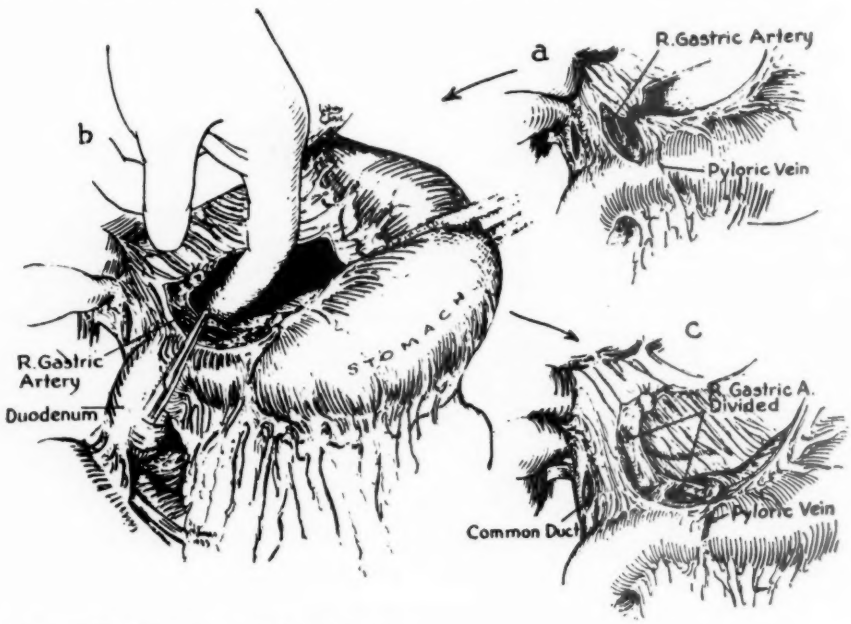

Fig. 3, *C*.—Technique of total gastrectomy.

(a) The lesser peritoneal cavity is opened through the gastrohepatic omentum. (b) The right gastric artery and vein are clamped close to the pylorus. (c) Vessels of the gastrohepatic omentum have been ligated and the lesser curvature is cleared. (From Lahey and Marshall.[33])

Type of Anastomosis.—After resection of the entire stomach the continuity of the gastrointestinal tract must be re-established by a direct anastomosis between the esophagus and the small intestine. The collective review of Pack and McNeer[47] shows that in the period from 1884 to 1930 this restoration was accomplished in about one-half of the cases by means of an esophagoduodenostomy. Both the duodenum and the esophagus were mobilized until an end-to-end anastomosis could be performed. Since 1930 this procedure has been largely abandoned. Although in some cases esophagoduodenostomy

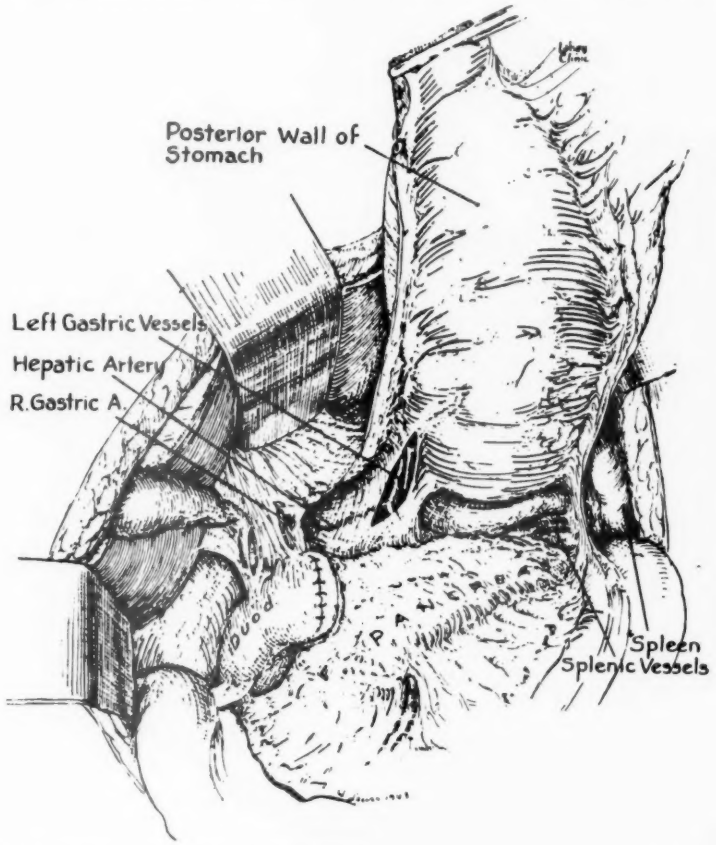

Fig. 3, *D.*—Technique of total gastrectomy.
The duodenum has been cut across and inverted, and the stomach has been lifted higher. Note the exposure of the left gastric vessels ready for ligation. (From Lahey and Marshall.[33])

is readily performed, the danger of excessive tension on the suture line is always present. Most surgeons prefer to close the duodenal stump in the usual way and to restore continuity by means of an end-to-side esophagojejunostomy. It is immaterial whether the jejunal loop is brought up anterior or posterior to the transverse colon, so long as a tension-free anastomosis is assured. If the anastomosis is made above the diaphragm it is usually advisable to use the retrocolic position and Sweet[65] has pointed out that it may be necessary in addition to lengthen the jejunal loop by dividing some of the mesenteric vessels (Fig. 5).

The formation of an entero-enterostomy between the proximal and distal jejunal loops is now advised by most of those who have had experience with

the operation.[3, 22, 26, 31, 48, 61, 73, 74] If the jejunum is brought behind the transverse colon the lateral anastomosis may be placed either above or below the transverse mesocolon. The advantages of such an anastomosis are: (1) the reduction of back pressure against the duodenal stump; (2) the avoidance of stasis of food in the proximal jejunal loop; (3) the elimination of regurgitation into the esophagus of irritating bile and pancreatic juice.

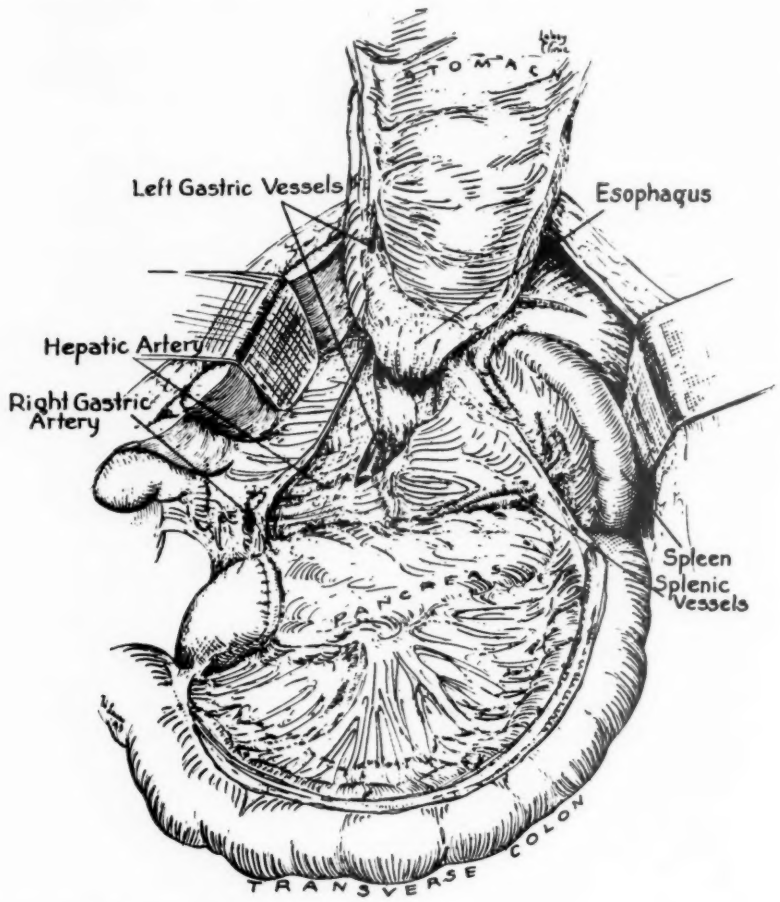

Fig. 3, *E*.—Technique of total gastrectomy.

The esophagus has been exposed and freed, the stomach has been turned up, and the pedicle of the spleen has been visualized. The left gastric vessels have been ligated. The spleen is ready to be removed with the stomach. (From Lahey and Marshall.[33])

When the jejunal loop is too short for a comfortable, tension-free anastomosis, one can use a modification of the Roux Y principle as adapted to esophagogastrostomy by Rienhoff,[58] Garlock,[19] and Orr.[46] Various applications of the method are discussed by Reynolds and Young.[57] A classical Roux Y is formed by dividing the jejunum near the ligament of Treitz, closing the distal limb and bringing the blind limb up behind the transverse colon for an end-to-side esophagojejunostomy. The proximal jejunal limb is then joined to the distal limb at a lower level by an end-to-side anastomosis. Alternatively, a longer arm of jejunum may be provided by dividing the jejunum lower down

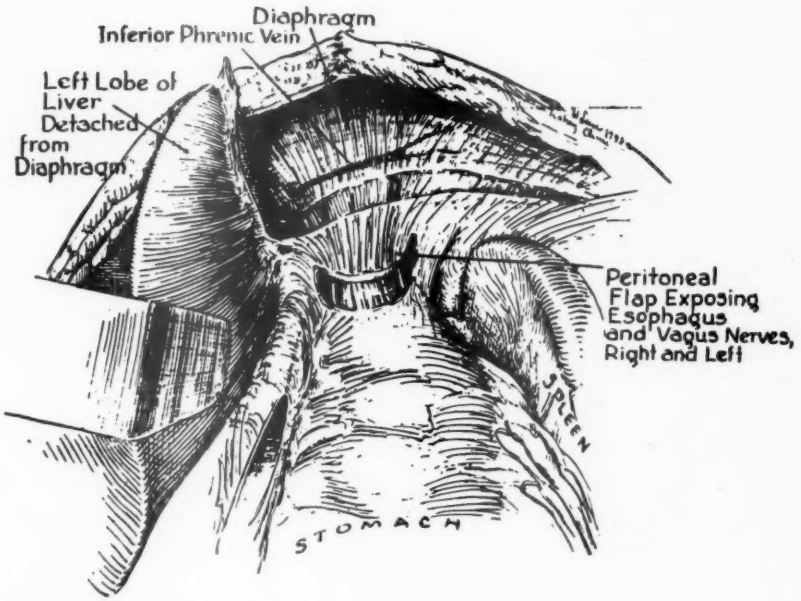

Fig. 3, *F*.—Technique of total gastrectomy.

The left lobe of the liver is mobilized to the right, and the anterior flap of the peritoneum is reflected up over the esophagus. This is used later to suspend the jejunum in order to remove traction from the anastomotic line. (From Lahey and Marshall.[33])

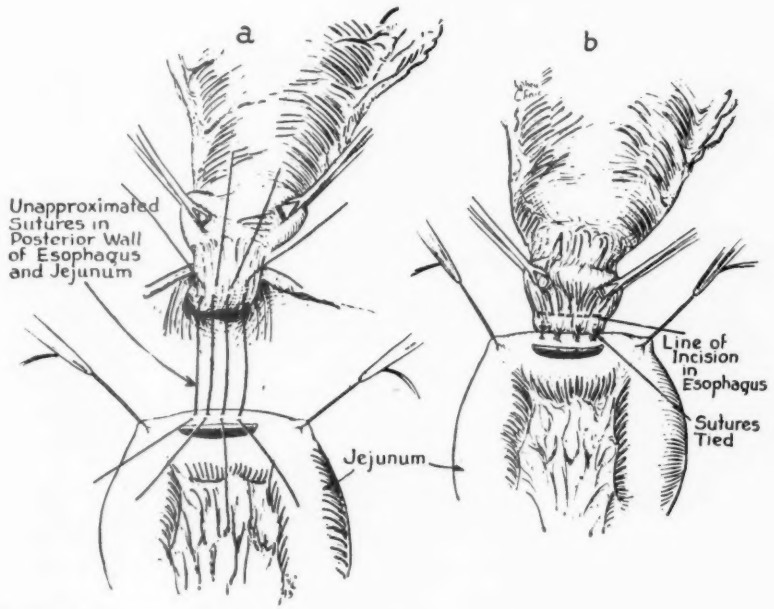

Fig. 3, *G*.—Technique of total gastrectomy.

(a) The preliminary introduction of a posterior row of untied silk sutures before opening the jejunum. Note the ease with which the jejunum may be opened and trimmed to fit the esophagus. (b) When the sutures are put in and tied before the jejunum is opened, satisfactory management as to size and fit of the jejunal opening is difficult with the jejunum pulled high up under the stomach. (From Lahey and Marshall.[33])

and using the proximal limb for the esophagojejunostomy. The advantages of the Roux Y procedure are: (1) the elimination of tension, even when a high intrathoracic anastomosis is necessary; (2) direct entrance of food into the jejunum without filling of the proximal loop; (3) elimination of distention or delay in emptying of the jejunum; (4) elimination of regurgitation of bile into the esophagus.

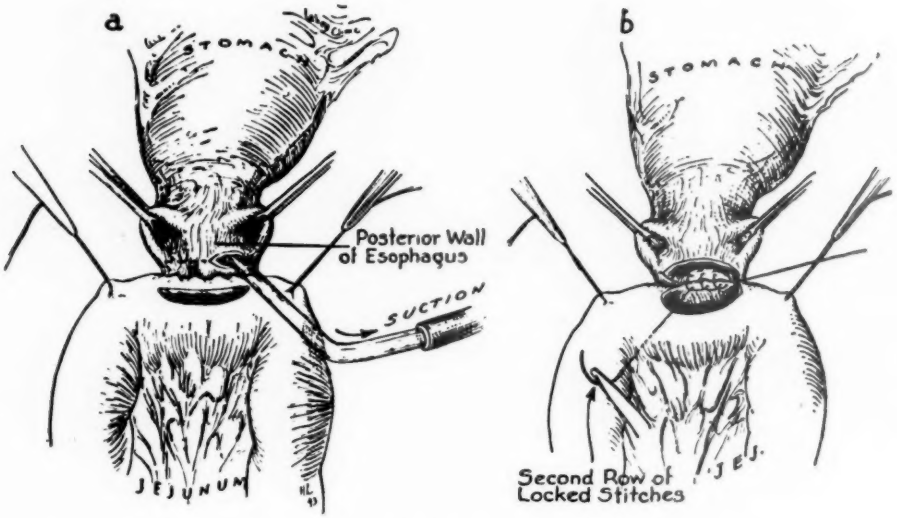

Fig. 3, *H*.—Technique of total gastrectomy.

(a) The traction stitches to hold the anastomotic opening are spread apart. The first row of silk stitches already has been tied. Note the small opening in the esophagus. (b) Note the locked stitches employed a step at a time as the opening gradually is increased in size until the entire posterior second row of stitches has been inserted. (From Lahey and Marshall.[33])

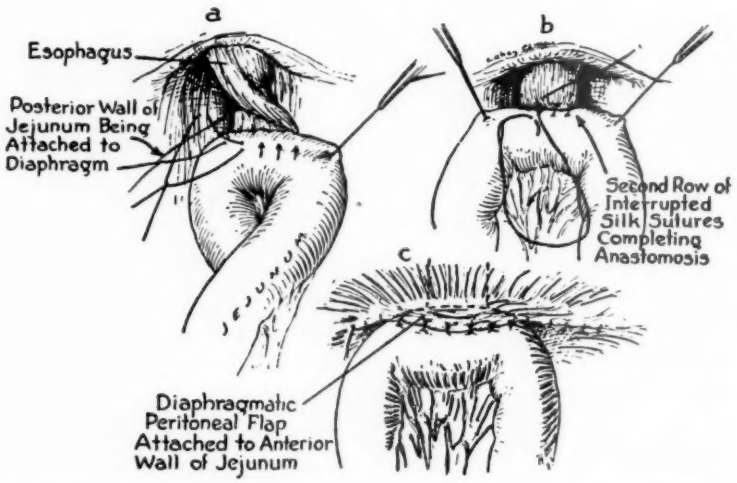

Fig. 3, *I*.—Technique of total gastrectomy.

(a) The method of twisting the esophagojejunal anastomosis in order to inspect the posterior row of sutures, and the insertion of suspensory jejunal sutures posteriorly to take the strain off the posterior row of anastomotic suture line. (b) The application of the anterior second row of silk approximation sutures. (c) The previously fashioned flap of diaphragmatic peritoneum sutured to the jejunum over the anastomosis to reinforce it, to suspend the jejunum and to relieve traction on the anastomotic line. (From Lahey and Marshall.[33])

Technique of Anastomosis.—The technical difficulties and dangers of esophagojejunostomy have been emphasized by all surgeons who have reported their experience with total gastrectomy. Some of the factors responsible for these difficulties are: (1) the relatively poor blood supply of the lower esophagus, particularly after it has been mobilized and drawn down into the abdomen; (2) the absence of a peritoneal covering of the distal esophagus

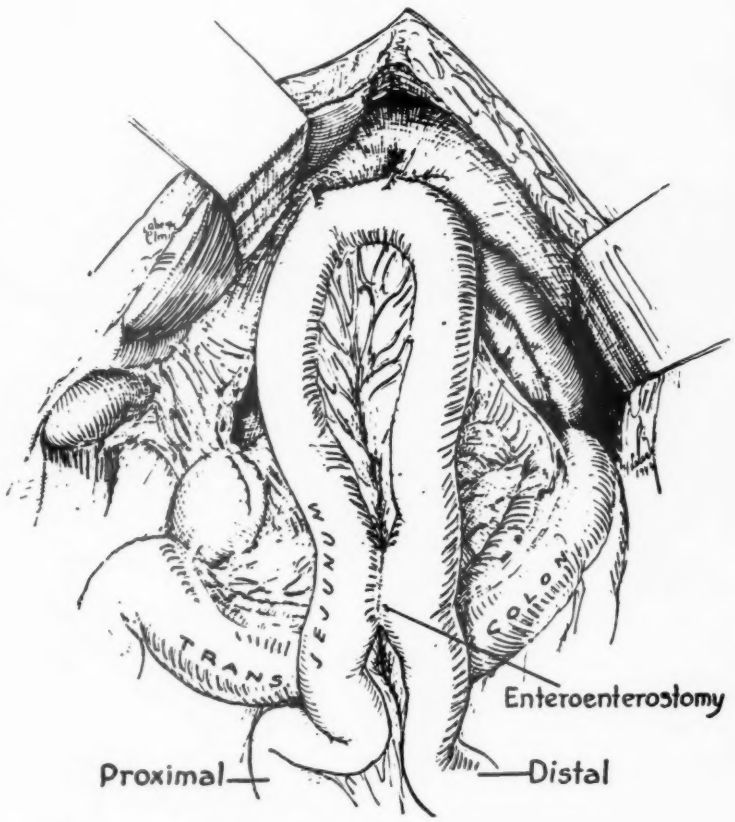

Fig. 3, *J.*—Technique of total gastrectomy.
The antecolic esophagojejunal anastomosis with additional suspension sutures to the diaphragm. Note the entero-enterostomy. (From Lahey and Marshall.[33])

and the friability of its muscular coat; (3) the technical disadvantage of forming the anastomosis high up under the diaphragm using a short segment of the esophagus; (4) the likelihood of some tension on the suture line due to inadequate length of the jejunal loop; (5) the contamination of the operative field due to the presence within the esophagus of oral secretions. Some of the methods devised by various surgeons to overcome these difficulties will be briefly reviewed.

1. Throughout the entire procedure the blood supply of the lower esophagus should be preserved with meticulous care. Mobilization of the esophagus should be carried out with the greatest of gentleness. Sweet[67] has emphasized the importance of consideration of the segmental blood supply of the esopha-

gus in order to avoid necrosis at the suture line. He advises that an anastomosis should never be performed more than 2 or 3 cm. below the nearest esophageal artery. No clamps should be used on the portions of the esophagus or the jejunum which are to be employed in the formation of the anastomosis.

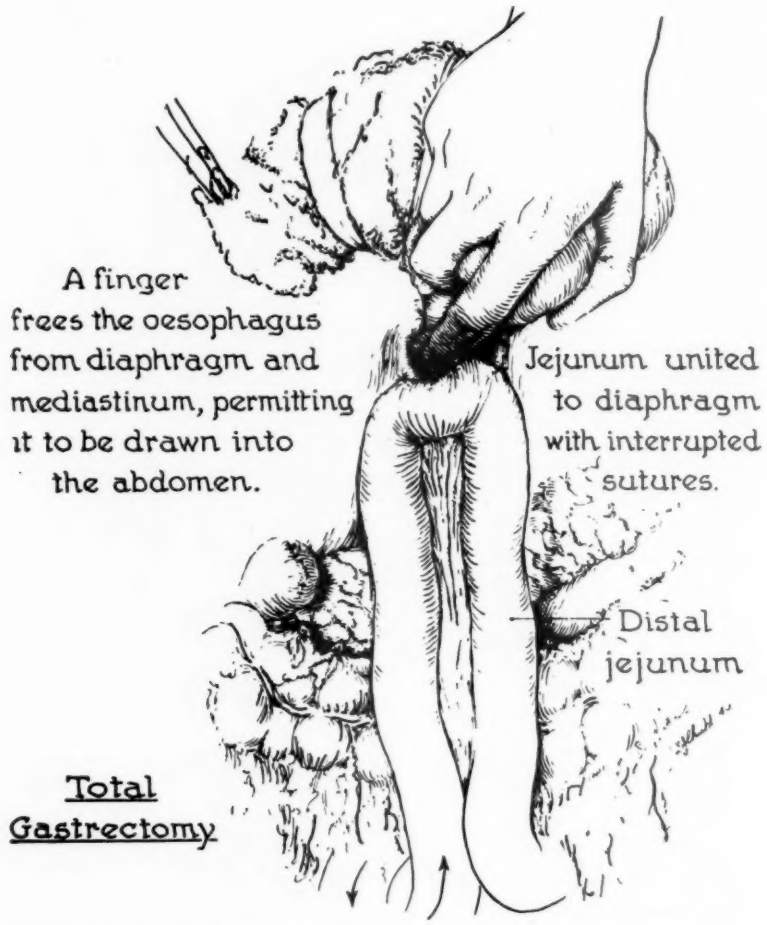
A finger frees the oesophagus from diaphragm and mediastinum, permitting it to be drawn into the abdomen.
Jejunum united to diaphragm with interrupted sutures.
Distal jejunum
Total Gastrectomy

Fig. 4, *A*.—Technique of gastrojejunostomy after total gastrectomy.
The stomach has been divided from the duodenum. The illustration shows the method of increasing the infradiaphragmatic length of the esophagus by freeing it from the margins of the diaphragm by inserting the finger along the esophagus into the mediastinum. The esophagus at a point eighteen inches from the duodenojejunal juncture is fastened to the diaphragm behind the entrance of the esophagus by means of interrupted sutures. (From Graham.[22])

2. The poor quality of the supporting tissues of the esophagus and the absence of a peritoneal covering demand the most meticulous care in the placement of sutures for the anastomosis. Until recently most surgeons have employed an inner continuous suture of fine chromicized catgut, including all layers of the esophagus and jejunum, and an outer seromuscular layer of mattress sutures of fine silk.[26, 33, 48, 54, 63, 74] Because of the tendency of continuous sutures to cause gathering and narrowing of the stoma, Churchill and Sweet[8, 9] suggested the use of an inner layer of interrupted sutures of fine silk for accurate approximation of the mucosa and an outer layer of mattress su-

tures of the same material for approximating the seromuscular wall of the jejunum or stomach and the muscularis of the esophagus (Fig. 2). This technique has been widely adopted by those who have recently reported their experience with esophagogastric anastomosis,[13, 20, 49, 51, 67] and is now recommended as the method of choice for esophagojejunostomy.[41, 57, 61, 73]

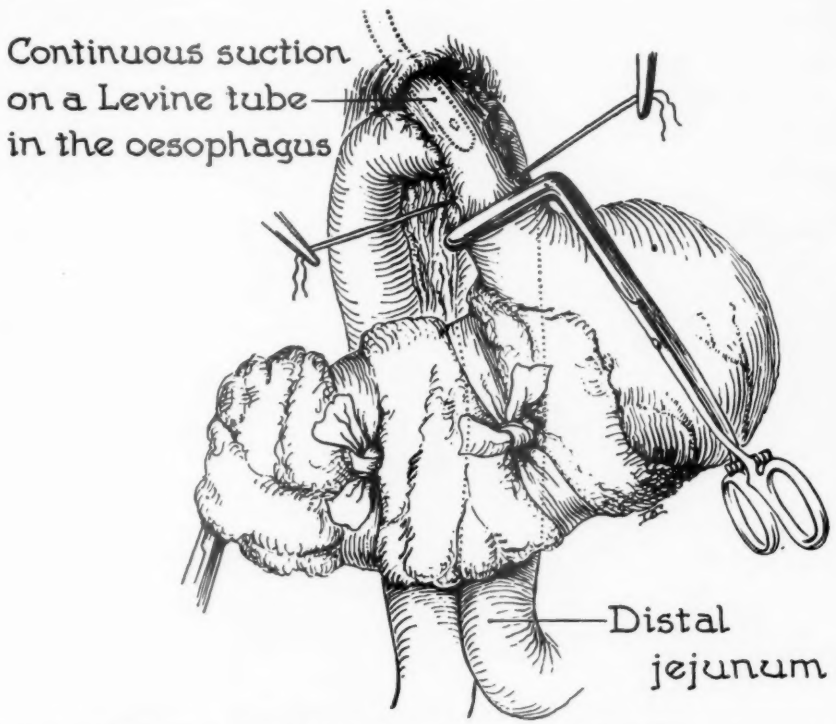

Fig. 4, *B*.—Technique of gastrojejunostomy after total gastrectomy.
The infradiaphragmatic portion of the esophagus is placed on the anterior surface of the distal limb of the jejunum and fastened there by means of interrupted silk sutures. The Levine tube in the esophagus by means of attachment to suction apparatus keeps the esophagus free from accumulated secretions. (From Graham.[22])

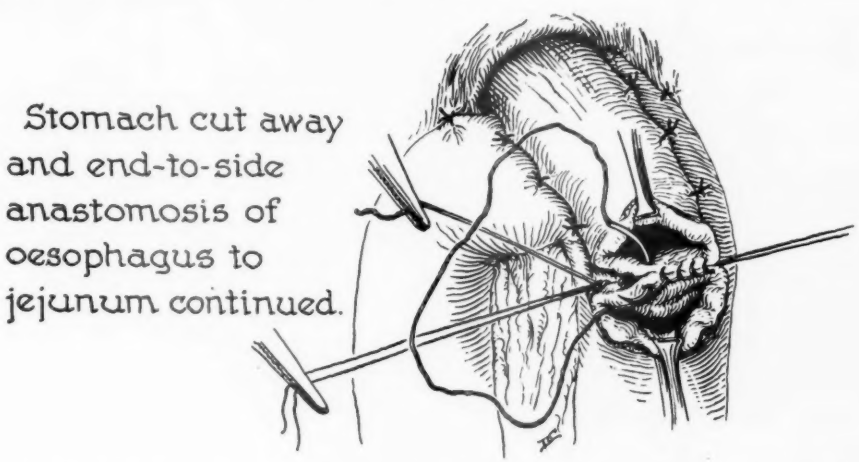

Fig. 4, *C*.—Technique of gastrojejunostomy and entero-enterostomy after total gastrectomy.
Here the stomach is cut away and the mucous membranes of the stomach and jejunum are being united. (From Graham.[22])

3. The difficulties of exposure are minimized by taking advantage of the maximal relaxation of spinal anesthesia, by use of an adequate incision, and by division of the triangular ligament and retraction of the left lobe of the liver. Pack and McNeer[47] and Lahey and Marshall[33, 40] have found it convenient to place the posterior row of interrupted mattress sutures with the jejunum at some distance from the upturned esophagus. The jejunum may then be slid along these sutures into position and the sutures tied down, maintaining the relationship of the esophagus and jejunum for the anastomosis (Fig. 3, *g*). If necessary, additional exposure should be obtained by means of the combined abdominothoracic approach. Although this procedure adds to the extent of the operation, it is frequently the only means of obtaining

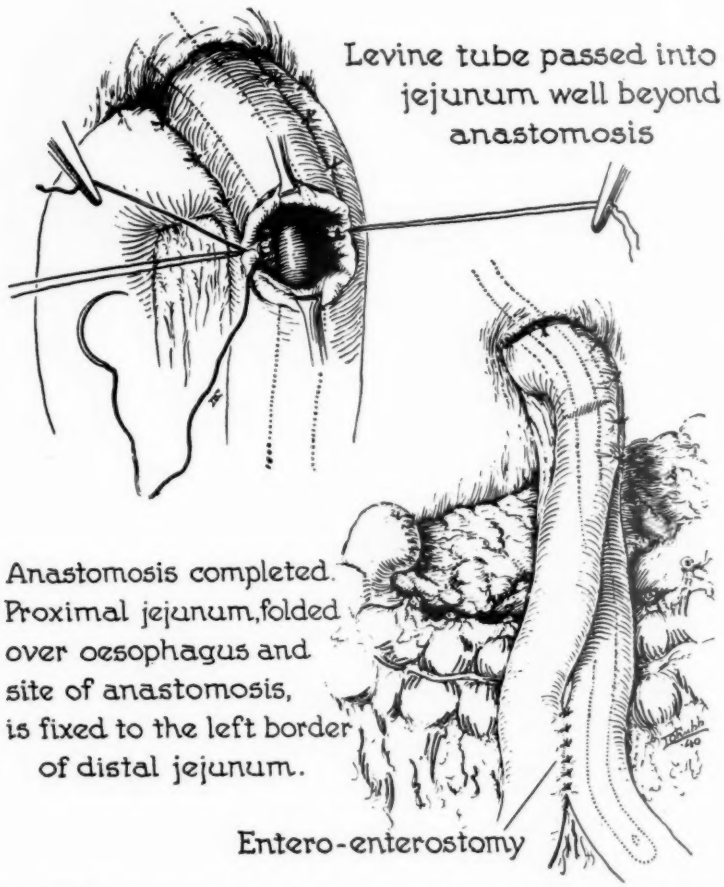
Levine tube passed into jejunum well beyond anastomosis
Anastomosis completed. Proximal jejunum, folded over oesophagus and site of anastomosis, is fixed to the left border of distal jejunum.
Entero-enterostomy

Fig. 4, *D*.—Technique of gastro-jejunostomy and entero-enterostomy after total gastrectomy.

When the posterior layer of mucous membrane sutures is completed, the Levine tube is passed down further into the distal jejunum well past the esophagojejunal anastomosis and the anterior layers of the anastomosis are completed. The proximal jejunum is then folded over the front of the esophagus and the esophagojejunal anastomosis and united to the lateral margin of the distal limb of the jejunum. By this maneuver the esophagus and the esophagojejunal anastomosis are completely encircled by the jejunal loops. This contact of peritoneum to peritoneum ensures healing to a greater degree than the contact of bare esophagus to the jejunum. This maneuver completely obstructs the proximal jejunal loop and makes an enteroanastomosis necessary. During this anastomosis the Levine tube is passed further down into the distal jejunum to make possible direct jejunal feeding early in the patient's convalescence. (From Graham.[22])

the exposure which is necessary for the performance of a secure and accurate anastomosis, and it should be employed without hesitation.

4. Tension on the suture line has been a constant source of worry after total gastrectomy. Pack and McNeer[47] credit Moynihan with first suturing the jejunum to the under surface of the diaphragm to protect the suture line. Various modifications of this important step have been stressed by a number of surgeons.[2, 44, 47, 54, 59, 70] Lahey[30] first prepared a peritoneal flap anterior to the esophageal hiatus and sutured this flap to the jejunum to minimize

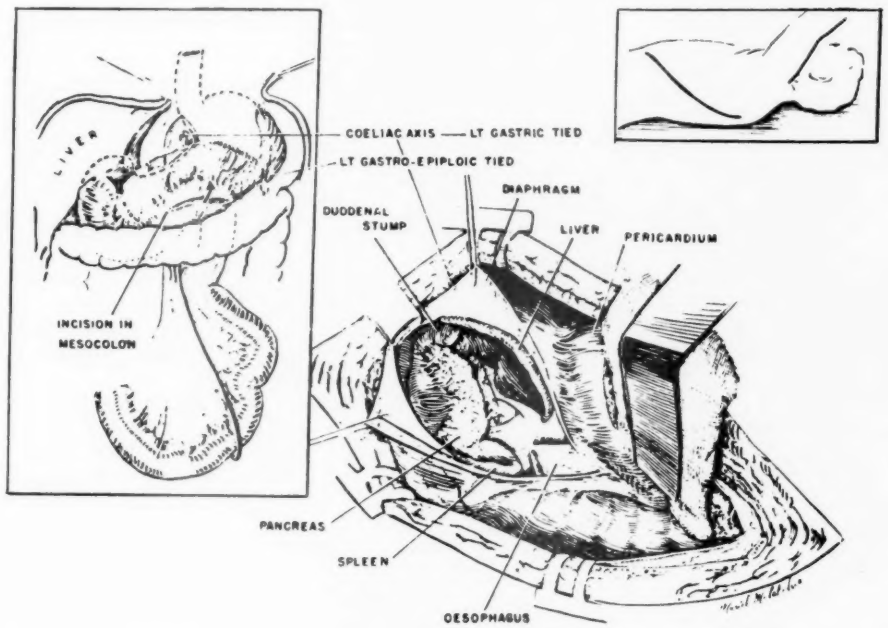

Fig. 5, *A*.—Technique of transthoracic total gastrectomy with lengthening of the jejunal mesentery.

General view of the field of operation after the stomach has been removed showing the lung retracted, the edges of the diaphragm parted, the duodenal stump sutured, and the cut end of esophagus ready for the anastomosis. Insert upper right shows the direction of the incision over the ninth rib on the left side. Insert to the left shows the level of transection of the esophagus above the diaphragm, the line of incision in the transverse mesocolon, and the proximal loop of jejunum which is to be used for the anastomosis. Note the vascular pattern in the mesentery of this loop. (From Sweet.[65])

tension and to reinforce the anastomosis (Fig. *3, f* to *i*). The procedure has been widely adopted. With the same objective Wangensteen[73] has added a posterior esophagojejunal buttress formed by a preliminary row of interrupted silk sutures anchoring the mesenteric border of the jejunum as a buttress against the posterior esophageal wall. In 1940 Graham[22, 23] reported a new techinque of esophagojejunostomy designed to afford additional support and protection to the suture line (Fig. 4). The esophagus is first secured parallel to the efferent limb of the jejunum by a few interrupted silk sutures. An end-to-side esophagojejunostomy is then performed, using a transverse incision in the jejunum. The afferent jejunal loop is finally folded over in such a way as to completely surround the anastomosis. Modifications of this type of anastomosis have been used with satisfaction by Sweet[65] and by

Smithwick.[63] If the transthoracic or abdominothoracic approach is used and the anastomosis is performed above the diaphragm, tension is effectively eliminated by suturing the diaphragm around the jejunal loop to provide secure support. Further stability may be obtained by crushing the left phrenic nerve to immobilize the left leaf of the diaphragm.[20, 51, 65]

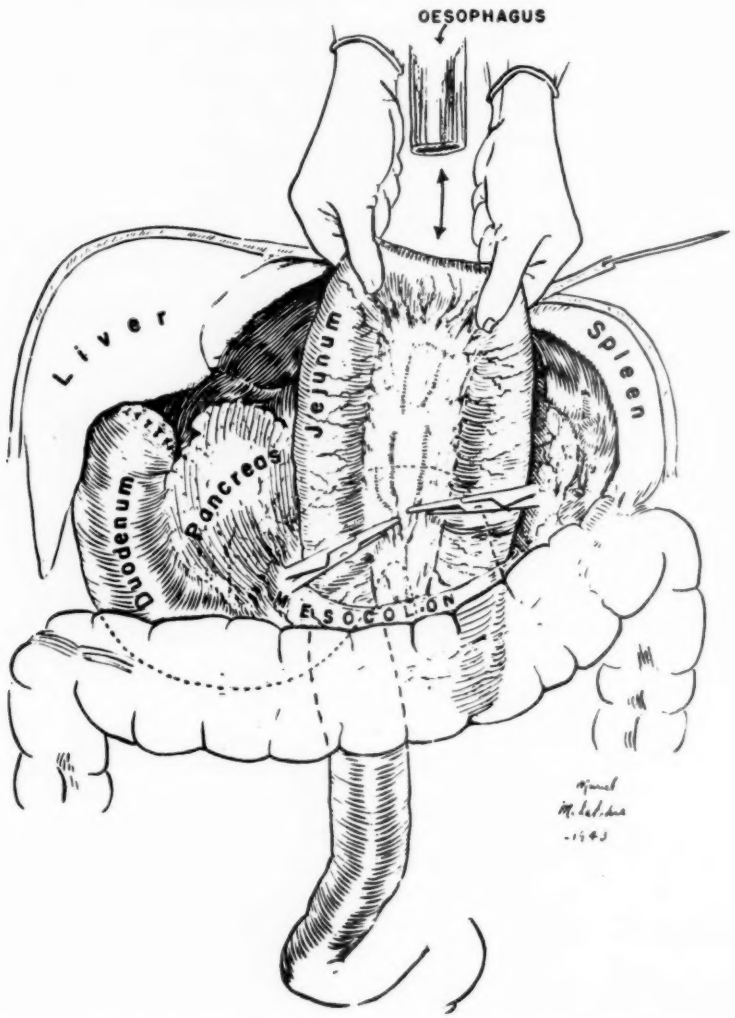

Fig. 5, *B*.—Technique of transthoracic total gastrectomy with lengthening of the jejunal mesentery.

Proximal loop of jejunum drawn up through the transverse mesocolon. The pull of the mesenteric vessels makes it possible to extend the apex of the loop much above the level of the diaphragm. Anastomosis with the esophagus not possible without release of the pull of the mesenteric vessels. Point of division of these vessels shown by hemostatic forceps in the drawing. (From Sweet.[65])

5. The fifth hazard of esophagojejunostomy is that of infection due to contamination of the operative field by organisms from the nasopharynx which are present in the opened esophagus. Smithwick in particular has emphasized this factor and has devised an ingenious aseptic modification of the Graham technique of anastomosis, employing a special thin-bladed anas-

tomosis clamp. The method has given good results in his hands, but most surgeons prefer an open type of anastomosis. Wangensteen[73] abandoned the closed anastomosis of the esophagus because of the high incidence of strictures encountered in his experience. In any case, the greatest care should be exer-

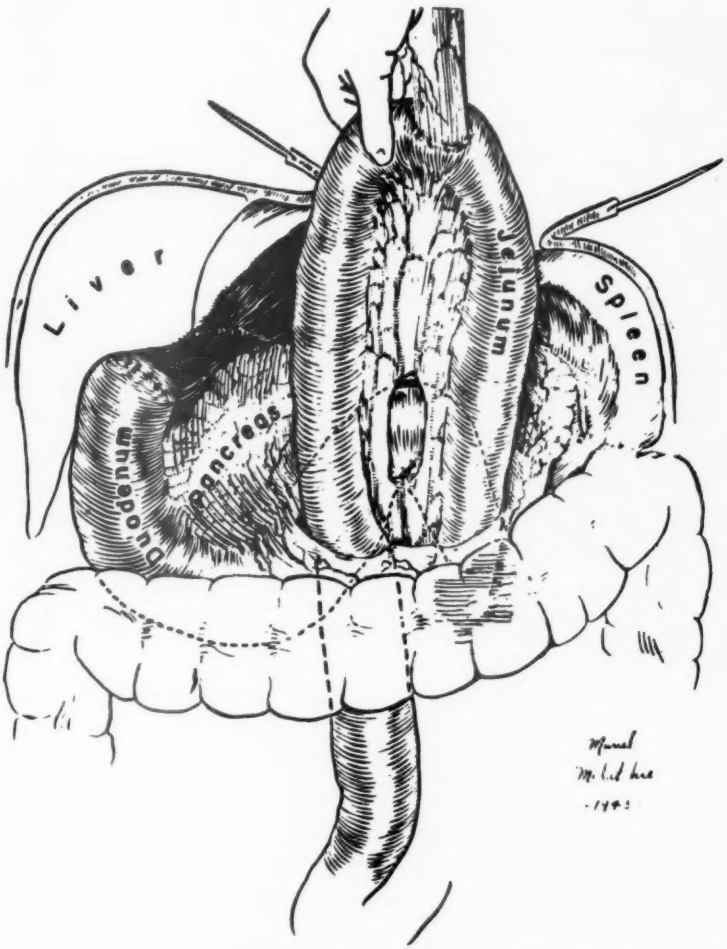

Fig. 5, *C*.—Esphogojejunostomy above the diaphragm after lengthening of the jejunal mesentery.

Marked release of tension after division of the mesenteric vessels makes it possible to bring the proximal loop of jejunum high above the diaphragm into the chest, and the esophagojejunostomy is performed without tension on its suture line. (From Sweet.[65])

cised to avoid gross soiling of the operative field. After completion of the anastomosis penicillin and streptomycin are instilled locally and the administration of these antibiotics is continued postoperatively by intramuscular injection. Wangensteen[73] felt that an important step in avoiding infection is the use of an air suction pump drain to prevent the accumulation of blood, serum, or pancreatic secretions in the region of the anastomosis.

POSTOPERATIVE MANAGEMENT

The general management of these cases is the same as that of any patient after a major laparotomy or thoracotomy, depending on whether the trans-

abdominal or transthoracic approach was used. Special attention should be paid to prophylaxis against pulmonary complications by encouraging frequent changes of position with deep breathing and coughing and by intermittent inhalations of a 7 per cent carbon dioxide and oxygen mixture. Continuous administration of oxygen may be required for 24 or 48 hours after transthoracic procedures. Pack and associates[48] advised the use of intercostal

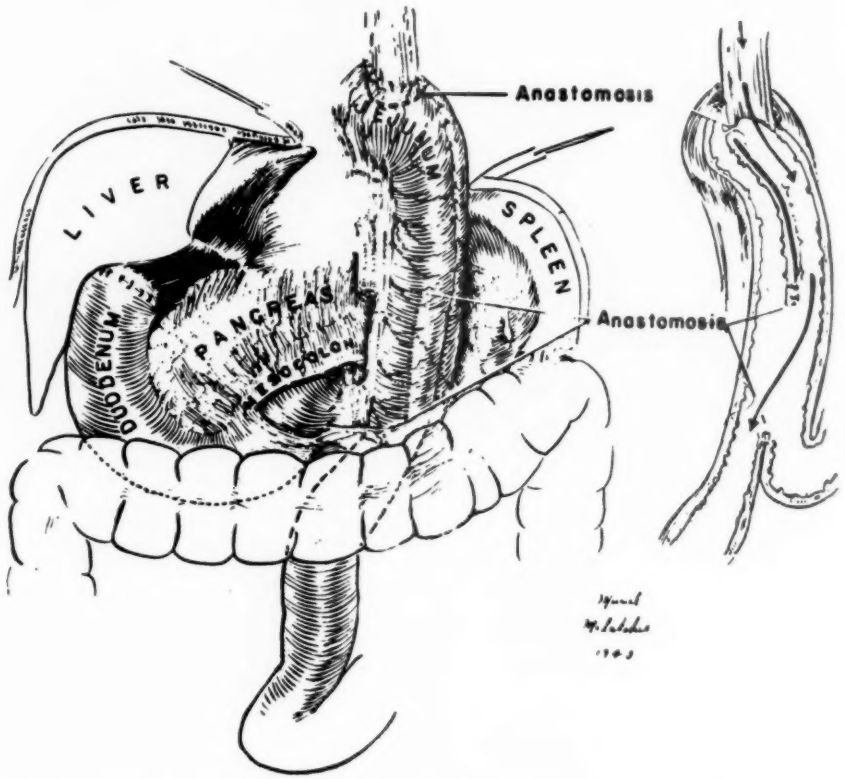

Fig. 5, *D*.—Esophagojejunostomy above the diaphragm after lengthening of the jejunal mesentery.

Completed anastomosis. Roscoe Graham technic used to reinforce the line of suture. Entero-enterostomy between the afferent and efferent arms of the jejunal loop shown just above the level of the opening in the transverse mescolon. Insert shows vertical section of lower esophagus and jejunal loop to which it has been anastomosed—entero-enterostomy shown. (From Sweet.[65])

nerve block with eucupine in oil as a prophylaxis against pulmonary complications, while Ransom[54] emphasized the importance of early recognition of postoperative atelectasis and vigorous treatment by intratracheal catheter suction or bronchoscopic aspiration. After thoracotomy and esophageal anastomosis within the thorax most surgeons routinely employ catheter suction drainage of the pleural space for 48 or 72 hours as a prophylaxis against atelectasis and pleural affusion.[13, 20, 49, 51, 67]

These patients, because of their age and general debility and the magnitude of the surgical procedure, are prone to venous stasis and thrombosis with subsequent pulmonary embolism. It will be noted from Table IV that pulmonary embolism accounted for 6.6 per cent of 45 deaths following total gastrectomy

collected from several recent reports. The legs of each patient should be examined several times daily and bilateral ligation of the superficial femoral veins should be performed, or anticoagulant therapy instituted, on the slightest evidence of phlebothrombosis or thrombophlebitis.

Because infection is the most frequent cause of death after total gastrectomy (Table IV), full use should be made of the newer antibiotic agents. The studies of Zintel[77] in experimental peritonitis indicate that a combination of streptomycin and penicillin is more effective than either of these agents alone or in combination with the sulfonamides. One million units of penicillin and 2.0 Gm. of streptomycin should be given daily in divided doses every 3 hours by intramuscular injection, commencing 24 or 48 hours before operation and continuing for at least 5 days after operation. The local use of these agents at the time of operation, as described by Sweet,[67] Garlock,[20] and others, appears to be a valuable adjunct to parenteral therapy.

The postoperative care of patients after total gastrectomy is complicated by 2 special factors: (1) the presence of a rather delicate esophagojejunal anastomosis, and (2) the need for a good nutritional intake during the early postoperative period. Until recently most surgeons did not allow a patient to take food or fluid by mouth for about a week after operation. Nutrition was provided by intrajejunal liquid feedings through a nasal tube introduced through the esophagojejunostomy into the distal jejunal loop at the time of operation, or by means of a separate jejunostomy performed as a supplementary part of the operative procedure.[47] Many surgeons have now abandoned this practice, for several reasons.[20, 26, 41, 63, 67] (1) It has been demonstrated that adequate fluid, electrolytes, calories, protein, and vitamins to maintain the patient in positive balance are readily provided intravenously for a period of several days.[28] (2) Prolonged suction at the site of the anastomosis is not necessary, particularly if a supplementary entero-enterostomy has been done. (3) The presence of the in-lying tube may increase the danger of necrosis at the suture line. The tube is therefore removed within 24 hours after operation and the patient is allowed to take liquids by mouth shortly thereafter. Oral intake is then gradually increased by the addition of thicker liquids, semisolid foods and solid foods, until a full diet, divided into 6 small feedings daily, is attained by about the tenth postoperative day. Until the nutritional intake by mouth is completely adequate, a positive balance is maintained by the parenteral administration of glucose, electrolytes, protein hydrolysate, plasma, blood, and vitamins as indicated.

POSTOPERATIVE MORTALITY

Recent years have witnessed a marked decline in the mortality associated with total gastrectomy. Table I, based on the collected series of Pack and McNeer,[47] shows the mortality rate during successive periods from 1884 to 1942. In the period 1931 to 1942, 166 cases were reported with 57 deaths, or a mortality rate of 34.3 per cent. Table II is based on reports of relatively large series of cases published since 1947. Most of these operations were performed

TABLE I. OPERATIVE MORTALITY OF TOTAL GASTRECTOMY, 1884 TO 1942 (PACK AND MCNEER[47])

	OPERATIONS	MORTALITY	
		NUMBER	PER CENT
1884-1920	75	37	49.3
1921-1930	57	18	31.6
1931-1942	166	57	34.3

during the 7 year period 1942 to 1949. It will be noted that in the total group of 276 cases of total gastrectomy there were only 44 deaths, or a mortality rate of 15.9 per cent. In the 2 large series of Scott and Longmire[61] and of Lahey[32] the mortality rate was approximately 10 per cent, while Wangensteen had only

TABLE II. OPERATIVE MORTALITY OF TOTAL GASTRECTOMY FOR CANCER, 1942 TO 1949

AUTHORS	YEAR	OPERATIONS	MORTALITY	
			NUMBER	PER CENT
Ransom[54]	1947	60	14	23.3
Pack, McNeer, and Booher[48]	1947	41	13	31.7
Scott and Longmire[61]	1949	63	6	9.5
Wangensteen[73]	1949	28	1	3.5
Lahey[32]	1950	58	6	10.3
Walters and associates[71]	1950	26	4	15.4
Total		276	44	15.9

1 death in a series of 28 total gastrectomies for cancer. It is of interest to compare these mortality figures with those for subtotal gastrectomy for cancer presented in 3 recent surveys covering a roughly corresponding period[50, 64, 75] (Table III). The mortality rate for the combined series of 499 operations is 11.2 per cent.

TABLE III. OPERATIVE MORTALITY OF PARTIAL GASTRECTOMY FOR CANCER, 1936 TO 1946

AUTHORS	PERIOD	OPERATIONS	MORTALITY	
			NUMBER	PER CENT
State, Moore, and Wangensteen[64]	1936-45	276	42	15.2
Welch and Allen[75]	1942-46	179	7	3.9
Pack and McNeer[50]	1942-46	92	9	9.8
Total		547	58	10.6

It is probably true, as suggested by Smithwick,[63] that an important factor in the gratifying reduction in mortality is improved technique resulting from the increased experience of individual surgeons with operation. Other factors are: improved preoperative preparation and postoperative care, improved anesthesia and supportive treatment during operation, use of sulfonamides, penicillin, and streptomycin, greater attention to the prevention and treatment of pulmonary complications, and better selection of patients for operation with a broadening of the indications for total gastrectomy.[62]

Table IV presents a comparison of the relative frequency of various causes of death in the series of Pack and McNeer[47] and in a group of 45 instances of

death following total gastrectomy collected from recent reports.[38, 48, 54, 62, 63, 66] As emphasized by Smithwick,[63] infection, including peritonitis, empyema, and mediastinitis, continues to be the major cause of death following total gastrectomy. Better anesthesia and supportive therapy have all but eliminated shock as a cause of death in the recent series. Pneumonia and atelectasis remain a threat in spite of penicillin and more alert prophylaxis against respiratory complications, while there has been a relative increase in the frequency of death due to pulmonary embolism.

TABLE IV. CAUSES OF DEATH FOLLOWING TOTAL GASTRECTOMY

	PACK AND MC NEER[47] 1900-1942 (93 DEATHS)	COLLECTED SERIES[38, 48, 54, 62, 63, 66] 1942-1947 (45 DEATHS)
Infection (peritonitis, empyema, mediastinitis)	50.7	62.7
Pneumonia and atelectasis	18.3	20.0
Pulmonary embolism	1.1	6.6
Shock	18.3	2.0
Cardiovascular complications	6.5	5.2
Other	5.1	3.5

METABOLIC AND HEMATOLOGIC ABNORMALITIES IN THE LATE POSTOPERATIVE COURSE

The late postoperative course of patients following total gastrectomy is a matter of great interest and has been the subject of several excellent studies.[14, 38, 39, 47, 56, 61, 62] Only a brief review of this material is possible within the scope of this paper.

Smith[62] has reviewed the signs and symptoms observed in 57 patients following discharge from the hospital after total gastrectomy. Table V is based on his report. Dysphagia, noted by 28 per cent of the patients, is usually caused by scar tissue at the site of the esophagojejunostomy and is remedied by dilatation. In some cases this symptom may indicate a recurrence of malignancy, but dilatation should always be attempted. Diarrhea was experienced by 17 per cent of the patients, but was usually of short duration. It is quite possible that this symptom is due to the interference with intestinal motility caused by division of the vagus nerve. Nausea and vomiting were transitory symptoms and were readily controlled by antispasmodics and the use of small, frequent feedings. Failure to gain weight was not a prominent complaint, appearing in only 12 per cent of the patients. It might be noted here that all of Scott and Longmire's[38, 61] patients showed a slight gain in weight, but none of them equalled the weight which was normal for him before the onset of gastric symptoms. This was true in spite of the fact that all of the patients had a good appetite and apparently were eating well. It was surmised that the feeling of epigastric fullness and heartburn after eating experienced by most of these patients caused them to eat smaller meals, and many of them omitted the

between-meal feedings which were advised. The anemia which was noted in several of the patients in Smith's[62] series was not studied in detail, but did not resemble a primary or macrocytic anemia of the type reported by some observers.

TABLE V. SIGNS AND SYMPTOMS OBSERVED IN 57 PATIENTS FOLLOWING DISCHARGE FROM THE HOSPITAL AFTER TOTAL GASTRECTOMY (SMITH[62])

SYMPTOMS	NUMBER OF PATIENTS
Dysphagia	16
Abdominal pain	14
Diarrhea	10
Nausea or vomiting	9
Failure to gain weight	7
Anemia	7
Regurgitation	5
Fullness and abdominal distress	5
Weight loss	4
Heartburn	3
Weakness	3
Hiccup	3
Anorexia	2
Sore tongue	2
Intestinal obstruction	2

The preceding discussion of clinical symptoms suggests two problems which require further study: (1) the possible occurrence of certain metabolic abnormalities, particularly in regard to the digestion and absorption of protein, fat, and carbohydrate, and (2) the occurrence, in some individuals, of anemia, which is occasionally of the macrocytic, hyperchromic variety. These problems have been extensively reviewed and carefully studied in 3 patients by MacDonald, Ingelfinger, and Belding.[39] Their studies were carried out on 2 patients who had survived total gastrectomy for 10 years and 3 years, respectively, and on one patient 5 years after total gastrectomy, splenectomy, and partial pancreatectomy.

From the standpoint of metabolism they found that in the patients who had total gastrectomy alone the pancreatic enzymes were normal and fat absorption on a low fat intake was not significantly impaired. Vitamin A tolerance curves showed a delayed, but otherwise normal, absorption of the vitamin. Glucose tolerance tests revealed an early, transient hyperglycemia. The general condition of these patients was excellent. On the other hand, the patient with total gastrectomy, splenectomy, and partial pancreatectomy experienced difficulty in maintaining weight, pancreatic enzymes were deficient, fat absorption was impaired, and the vitamin A tolerance curve was flat. The glucose tolerance curve showed a sustained hyperglycemia.

These observations are in agreement with those of Farris and associates,[14] who found no abnormality in the absorption of fat or protein in a patient studied 4 years after total gastrectomy. They noted that the hyperglycemia of the glucose tolerance test might be followed by a rather marked hypoglycemia. Milanes and associates[43] also found no significant abnormalities of digestion or absorption in the 4 patients studied by them. All of the patients were in good general condition and no deficiency of hepatic or pancreatic function could be

demonstrated. Other investigators, however, have found definite impairment in the digestion and absorption of fat in all cases, although the metabolism of protein did not appear to be consistently affected.[38, 56] It has been suggested that this defect is due to hypofunction of the pancreas, secondary to section of the vagi, or to absence of acid gastric juice to stimulate the liberation of secretion by the duodenal mucosa.[25]

The changes in the blood picture after total gastrectomy are of particular interest in the light of the observations of Castle,[7, 16] suggesting that in man the stomach is the only source of the intrinsic antianemia factor. In a careful review of the literature on this subject, MacDonald and associates[39] found that, of 46 patients surviving for 3 years or more after total gastrectomy, 12 developed a blood picture resembling that of pernicious anemia. Two of their own 3 patients developed a macrocytic, hyperchromic type of anemia 2 and 5 years, respectively, after total gastrectomy. They concluded that: "The evidence appears to support the statement that an anemia morphologically similar to addisonian pernicious anemia will develop after total gastrectomy if the patient survives long enough."

On the other hand, Pack and McNeer,[47] Smith,[62] Ransom,[54] and Waugh and Fahlund[74] observed a pernicious anemia-like blood picture only very rarely in their relatively large groups of cases, whereas a hypochromic, microcytic type of secondary anemia was seen quite frequently. Farris and associates[14] considered that this iron-deficiency anemia results from the absence of the hydrochloric acid of the gastric juice, which normally converts ferric iron to ferrous iron for absorption. This type of anemia is prevented by the administration of 0.32 Gm. of ferrous sulphate 3 times a day for 1 week out of each month.

In summary, therefore, it seems to be established that there are 2 types of anemia which may appear after total gastrectomy: (1) a hypochromic, microcytic anemia which may appear early and is readily corrected by the use of ferrous iron; (2) a hyperchromic, macrocytic anemia which may not appear until 3 years or more after operation and responds only to the administration of liver extract or folic acid.

It is apparent from this brief review that patients who have been subjected to total gastrectomy present problems associated with the adequate intake and absorption of food and formation of the blood elements which require careful follow-up and close supervision. Longmire[38] reported 2 patients who died of starvation after leaving the hospital because of inadequate care at home and failure to follow the prescribed dietary regime. Smith[62] listed inanition as the cause of death of 7 of his patients who succumbed after leaving the hospital. To prevent such complications these patients should be seen and evaluated at frequent intervals after discharge. A high-protein, high-carbohydrate diet of adequate caloric value should be prescribed and should be divided into 5 or 6 daily meals. Generous vitamin supplements should be added. The weight and serum protein level should be followed as an index of the nutritional status of

the patient. A complete blood count should be done at regular intervals and secondary anemia should be treated by the administration of ferrous sulphate as required. If a macrocytic, hyperchromic type of anemia should appear, complete studies of the peripheral blood and bone marrow should be made, followed by liver or folic acid therapy if indicated.

END RESULTS

The end results of total gastrectomy for malignant tumors of the stomach have been discouraging, although one must constantly bear in mind the fact that in the past the operation has been applied only to patients with extensive and far-advanced disease, for whom the chance of cure has been quite remote.

In their review of 298 total gastrectomies for carcinoma, from 1884 to 1942, Pack and McNeer[47] were able to report only 16 patients who had lived over 3 years after operation. There were no 5 year survivals in this series. The recent report by Smith[62] of the end results of 88 total gastrectomies for malignant lesions performed at the Lahey Clinic from 1927 to 1945 is more encouraging. Sixty-three patients survived operation, and of these 12 patients lived for 3 years or more after operation. Three patients are living and well more than 5 years after total gastrectomy for leiomyosarcoma in one case, lymphosarcoma in the second case, and carcinoma in the third case. On the basis of these results Smith estimated that after total gastrectomy for malignant lesions 50 per cent of the patients will survive for 12 months, 30 per cent will survive for 18 months, 20 per cent will survive for 24 months, and 15 per cent will survive for 36 months.

Ransom[54] reported similar end results in a series of 55 total gastrectomies for malignant lesions. Of the 42 patients who survived operation, 31 subsequently died—approximately one-third of them in less than 6 months, one-third in from 6 to 12 months, and one-third in from 12 to 18 months. Eleven patients are still living, although 2 of these show evidence of recurrence. Three patients are living and well from 4 years and 5 months to 7 years and 11 months after operation and may be regarded as 5 year survivals. Smithwick[63] reported that of 9 patients on whom total gastrectomy was performed for carcinoma, 2 are living and well 10 years and 6 months and 5 years and 2 months after operation, respectively.

In summary it may be said that, out of a combined total of 153 patients subjected to total gastrectomy for malignant lesions included in the preceding reports, there were 8, or 5.2 per cent, who survived for 5 years or more after operation. This figure is discouragingly low, but one must bear in mind the fact that these are the "hopeless" cases, which would be considered inoperable by ordinary standards. It is to be expected that results will be improved as the indications for total gastrectomy are widened and as the technique of the operation is further standardized.

DISCUSSION

An attempt has been made to review the information presently available on the subject of total gastrectomy. In seeking to arrive at a fair judgment of

the present status of the operation in the treatment of gastric cancer it remains to examine, in the light of this information, the questions suggested at the beginning of the article.

Can total gastrectomy be performed with a mortality rate comparable to that of partial gastrectomy and, if so, what factors are important in attaining such results? Radical total gastrectomy, as described in this report, is unquestionably a more extensive and a more exacting operation than partial gastrectomy. It is also a newer operation with which the average surgeon has had only a very limited experience because it has been reserved for rare instances of very extensive, but still operable, gastric cancer. Nevertheless, the recent experience of a few surgeons with relatively large series of cases demonstrates that total gastrectomy can be performed with a mortality rate in the neighborhood of 10 per cent, a figure which is comparable to that for partial gastrectomy for cancer. These operations were, of course, performed by highly competent surgeons with a special interest in total gastrectomy and with the best facilities for patient care available in large centers. However, their results are an impressive demonstration of what can be accomplished. We have reviewed some of the points in operative technique, pre- and postoperative care and selection of patients which are of importance in attaining such results.

Can patients surviving after total gastrectomy maintain a reasonable state of nutrition, general health, and comfort over a period of years? The observations collected in this review would indicate that this question can be answered in the affirmative. The problems of digestion, nutrition, and anemia are not serious as long as the patient follows a carefully regulated routine and adequate supervision is maintained. The inconvenience or disability is perhaps comparable to that of the arm after radical mastectomy or of the colostomy after abdominoperineal resection—a small price for the patient who has been freed of cancer.

Is there a reasonable hope of increasing the curability rate by the application of the principles of radical gastrectomy in all cases of gastric cancer? This question is the crux of the argument for or against total gastrectomy as the standard operation for all gastric cancer, large or small. If one were convinced that more 5 year cures would result from such a practice, he would unhesitatingly accept the more formidable operation with its higher mortality rate and increased disability, just as one accepts radical mastectomy rather than simple mastectomy as the treatment for even the smallest of breast cancers.

Unfortunately, the evidence now at hand seems insufficient to answer the question. The survival rates quoted in this review are based on series of operations performed for far-advanced or "hopeless" cases of gastric cancer. Operations for earlier lesions are too recent to provide data on end results.

It is true that total gastrectomy, with removal en bloc of the greater omentum, the spleen, and all of the perigastric lymphatics, seems to be an operation more in keeping with our concepts of the surgery of cancer elsewhere in the body, that is, the lip and mouth, the breast, the lung, the colon and rectum.

It is also true that unrecognized intramural extension of gastric cancer is a cause of failure in some cases after partial gastrectomy, which would be eliminated by total resection of the stomach. On the other hand, the primary lymphatic drainage of the stomach is by a very short route to the region of the celiac axis, a structure which cannot be sacrificed and from which the lymph nodes are removed only with great difficulty. The tumor also has a great tendency to spread by invasion of veins and metastasis to the liver. One may argue on this basis that total gastrectomy and more extensive removal of lymphatics, other than those of the celiac axis itself, would result in very few more 5 year cures.

Additional information is obviously required and several lines of investigation suggest themselves. Of great value would be further studies of lymph node metastases similar to those reported by Gilchrist and David[21] for cancer of the colon. Careful post-mortem study of patients who died shortly after partial gastrectomy for cancer would show whether there remained lymphatic or intramural extension of the tumor which would have been removed by total gastrectomy. Another approach to the problem is that of Scott and Longmire[61] and Lahey,[32] who take the position that total gastrectomy has become a sufficiently safe and standardized procedure that it should be adopted on a trial basis as the standard operation for gastric cancer by a number of qualified surgeons in centers with optimum facilities for diagnosis, care, and follow-up of patients. Ten years from now, careful analysis of the collective experience of these surgeons will determine the true status of the operation.

CONCLUSIONS

1. Total gastrectomy is now a fairly well standardized procedure, with an operative mortality rate of 10 to 20 per cent when employed in the treatment of gastric cancer. With careful supervision patients may live a relatively normal life for many years after total resection of the stomach.

2. The operation is specifically indicated in the treatment of all operable gastric cancers the extent or location of which prevents adequate removal by partial gastrectomy. All general surgeons should be familiar with the technique of total gastrectomy and should employ this operation without hesitation in any situation in which the adequacy of partial gastrectomy seems open to question.

3. Evidence available at present is not sufficient to warrant the general adoption of total gastrectomy as the standard operation for all types of gastric cancer, early or advanced. However, it does seem reasonable that such a policy should be adopted on a trial basis by a number of qualified surgeons in well-organized centers so that data may be accumulated which will define the future status of total gastrectomy in the treatment of gastric cancer.

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Erratum

In Table I, on page 837 of the June, 1951 issue in the article "The Cystic Duct Stump Syndrome" by John H. Garlock and Elliott S. Hurwitt, the subhead under "Stones" should read "common duct" rather than "cystic duct." In Table II, on page 838 in the same article, the subheads under "Stones found in" should read "stump and common duct" rather than "stump and cystic duct" and "common duct only" rather than "cystic duct only."

Book Reviews

A Syllabus of Laboratory Examinations in Clinical Diagnosis: Critical Evaluation of Laboratory Procedures in the Study of the Patient. Edited by Thomas Hale Ham, B.S., M.D., Assistant Professor of Medicine, Harvard Medical School, Associate Director, Thorndike Memorial Laboratory, Junior Visiting Physician, Boston City Hospital. Pp. 496, with numerous illuustrations and tables. Price $5. Cambridge, Mass., 1950, Harvard University Press, Randall Hall.

This Syllabus, representing the work of 33 contributors, presents, first, an introduction to laboratory examinations which includes tables of normal values, estimated cost of laboratory examinations, and evaluation of data in general. The remaining units or sections are devoted to the following: (1) laboratory examinations of blood; (2) laboratory examinations related to the urinary system; (3) laboratory tests related to diseases of the gastrointestinal tract; (4) special tests related to infectious diseases; (5) special tests related to diseases of metabolism; and (6) special tests related to extravascular fluids. In each of these sections the laboratory examinations are discussed from the standpoint of "principle, method, and limitations and interpretations of the test itself and as a diagnostic aid related to the history and physical examination of the patient."

While this book presents the subject with clarity it is limited in scope and should serve only as a supplement to the excellent textbooks of clinical laboratory medicine.

Die Wiederherstellungs-Chirurgie. By K. E. Herlyn, Gottingen, insbesondere die Verwendung der Roll-Lappenplastik, 1949, XII/200 Seiten, 357 Abb. und 1 mehrfarb. Tafel. Pp. 200 with many illustrations. Stuttgart, 1949, Georg Thieme Verlag. American agents Grune & Stratton, Inc., New York. DM 32 (about $6.00).

This book is based upon the author's work during many years of peace and war. He is largely concerned with the use of the pedicled graft. The basic principles involved in using such grafts are clearly and simply presented. Following this, the application of the method in the repair of defects in the face and extremities is discussed. A large number of excellent photographs and diagrams illustrate the procedures employed and the end results attained. This book is a record of a real accomplishment and can be read with profit by those interested in reconstructive surgery.

Post Graduate Lectures on Orthopedic Diagnosis and Indications. Vol. I. Propedeutics in Orthopedic Diagnosis and Congenital Deformities and Disabilities. By Arthur Steindler, M.D., F.A.C.S., Professor of Orthopedic Surgery, State University of Iowa, Iowa City, Ia. Pp. 289, with many illustrations. Hard. Springfield, Ill., 1950, Charles C Thomas, Publisher. $7.50.

The author's preface characterizes this slim volume as a group of lectures intended to cover diagnosis and indications based upon thirty years of experience as a teacher and clinician. Technical procedures are not discussed. Writing clearly and concisely, and using ample illustrations, Dr. Steindler presents in the first section discussions of bodily symmetry and asymmetry, joint motion, gait, and the interpretation of pain in orthopedic conditions. The second section is composed of a review of congenital deformities and conditions.

The organization of the material is superb; the style is simple and straightforward. The entire book is thoroughly annotated and an excellent bibliography accompanies each section. This book could furnish a base for the instruction of students at any level. The projected volumes in this series will be eagerly awaited and the entire work, if the excellence of the initial volume is maintained, will set a new standard for orthopedic pedagogy.